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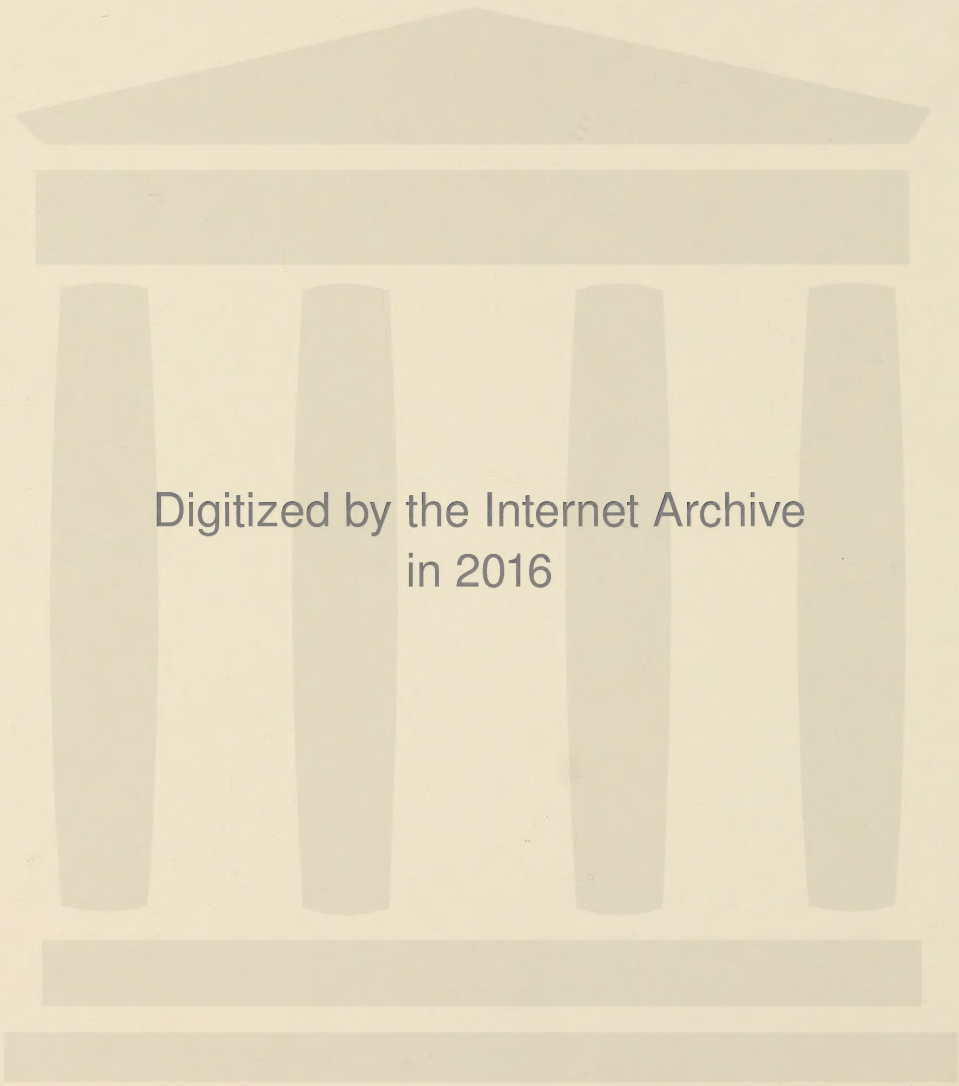
Surgical Treatments for Deep Venous Incompetence

Ann Scott and Paula Corabian

July 2003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Surgical Treatments for Deep Venous Incompetence

Executive Summary

Objectives

To critically appraise and synthesise the published evidence regarding the short- and long-term efficacy/effectiveness of surgical techniques for patients with deep venous incompetence, and attendant skin changes/ulceration, that is refractory to standard care. The information will be used to inform Health Ministry decisions regarding the reimbursement policy for such surgery within Alberta.

Background

Chronic venous disease affects up to 2% of the population in Western countries, a prevalence rate similar to that of diabetes. Chronic venous insufficiency (CVI) may either be of primary (idiopathic) or secondary (post-thrombotic) origin. In primary disease, valvular incompetence is caused by abnormalities of the venous wall and the valves. Secondary disease, the most common cause of CVI, results from thrombosis or post-thrombotic damage within the deep veins, which lead to vein obstruction or valvular incompetence. CVI is associated with retrograde venous blood flow and venous hypertension in the lower limb. This can generate vessel dilation, elongation and tortuosity; skin changes, edema, tissue malnutrition and eventual ulceration. Venous ulceration is a highly chronic condition with about 50%, 20% and 8% of ulcers not healed after 4 months, 2 years and 5 years, respectively. Overall, 25% of ulcers recur within one year.

CVI has considerable socioeconomic impact. The quality of life of patients suffering CVI is often extremely impaired, and the management of chronic wounds places an enormous economic burden on the healthcare system.

Methodology

All original, published studies on non-pregnant human patients undergoing treatment for deep or mixed deep/superficial/perforator CVI were identified by searching PubMed, EMBASE, CINAHL, The Cochrane Library, Science Citation Index, and the web sites of various health technology assessment agencies, research registers and guidelines sites from January 1990 to July 2003. Randomised controlled trials and non-randomised comparative studies were included, and no language or date restriction was applied.

Results

Two randomised controlled trials and 12 non-randomised comparative studies reported on a variety of procedures ranging from superficial venous surgery (SVS) and subfascial endoscopic perforator surgery (SEPS) through to deep venous reconstruction (including

valvuloplasty, transplantation and transposition) for the treatment of deep venous incompetence. However, deficiencies in reporting, methodological weakness and marked inter-study heterogeneity with respect to patient selection, postoperative management, surgical technique, definition of abnormal venous hemodynamics, symptom grading and diagnostic and venous function testing precluded any definitive synthesis of the data.

Limited evidence suggested that combined SVS/valvuloplasty is a relatively safe procedure that is potentially more effective than SVS alone in preventing ulcer recurrence in patients with primary deep venous incompetence in both the short- and midterm. Evidence for the efficacy of valvuloplasty, bypass, transplantation, SEPS and iliac stenting in the treatment of deep venous incompetence was inconclusive. The optimal surgery for patients with deep venous obstruction or secondary valvular incompetence remains unclear.

Conclusions and Recommendations

It is unlikely that a large randomised, or even non-randomised, controlled trial will be conducted to ascertain the safety and efficacy of surgery for deep venous incompetence because the complexity and long-term nature of CVI, plus the small proportion of CVI patients with refractory ulcer, make patient selection and ethical surgical comparison problematic. However, standardised reporting and collection of data in a registry would be a move forward. In addition, professional bodies such as The Royal College of Physicians and Surgeons of Canada should consider providing guidance, in the form of an evidence based treatment algorithm, that would define when to perform SVS in patients with mixed or deep venous incompetence and what type of deep venous surgery is considered appropriate for different indications.

Given that controversy still surrounds many aspects of CVI, it is clear that further good quality research is urgently needed. While it is important to know whether surgery for deep venous incompetence is efficacious and durable, it is equally important to quantify why less invasive treatments have failed in patients requiring surgery for deep venous incompetence.

Reference:

Scott A, Corabian P. Surgical treatments for deep venous incompetence. Edmonton, AB: Alberta Heritage Foundation for Medical Research; July 2003. (HTA 32: Series A).

The full text is available at http://www.ahfmr.ab.ca/programs.html

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HTA 32 Health Technology Assessment

Surgical Treatments for Deep Venous Incompetence

Ann Scott and Paula Corabian

July 2003

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This Health Technology Assessment Report has been prepared on the basis of available information of which the Foundation is aware from public literature and expert opinion, and attempts to be current to the date of publication. It has been externally reviewed. Additional information and comments related to the report are welcome and should be sent to:

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Tel: 780-423-5727, Fax: 780-429-3509

ISBN 1-896956-61-0 (Print)
ISBN 1-896956-63-7 (On-line)

ISSN 1704-1090 (Print)
ISSN 1704-1104 (On-line)

Alberta's Health Technology Assessment program has been established under the Health Research Collaboration Agreement between the Alberta Heritage Foundation for Medical Research and the Alberta Health Ministry.

ACKNOWLEDGEMENTS

The Alberta Heritage Foundation for Medical Research is grateful to the following persons for provision of information.

Dr. Franco Leoni, Smith Clinic, Camrose, Alberta

Ms. Maria Ospina, University of Alberta, Alberta

The Alberta Heritage Foundation for Medical Research is also grateful to the following persons for comments on the draft report.

Ms. Sue DeVries, Vascular Surgery, Toronto General Hospital, Toronto, Ontario

Dr. Tom Forbes, Division of Vascular Surgery, London Health Sciences Centre, London, Ontario

Mr. Simon Hardy, Department of Surgery, Blackburn Royal Infirmary, Blackburn, United Kingdom

Information Services Support

Ms. Leigh-Ann Topfer, Canadian Coordinating Office for Health Technology Assessment, Edmonton, Alberta

The views expressed in the final report are those of the Foundation.

SUMMARY

- The aim of this report was to critically appraise and synthesise the published evidence regarding the short- and long-term efficacy/effectiveness of surgical techniques for patients with deep venous incompetence, and attendant skin changes/ulceration, that is refractory to standard care.
- Chronic venous disease affects up to 2% of the population in Western countries, a prevalence rate similar to that of diabetes. Venous hypertension in the lower limb can be caused by reflux, venous obstruction or both, while venous pathology can be superficial (the most common), deep or mixed. Chronic venous insufficiency (CVI) may either be of primary (idiopathic) or secondary (post-thrombotic) origin. In primary disease, valvular incompetence is caused by abnormalities of the venous wall and the valves. Secondary disease, the most common cause of CVI, results from thrombosis or post-thrombotic damage within the deep veins, which lead to vein obstruction or valvular incompetence. CVI is associated with retrograde venous blood flow and venous hypertension in the lower limb.
- Chronic venous hypertension can generate vessel dilation, elongation and tortuosity; skin changes, edema, tissue malnutrition and eventual ulceration. Venous ulceration is a highly chronic condition with about 50%, 20% and 8% of ulcers not healed after 4 months, 2 years and 5 years, respectively. Overall, 25% of ulcers recur within one year. In the worst cases, ulcers can become infected and gangrenous, and may require amputation.
- CVI has a considerable socioeconomic impact. The quality of life of patients suffering CVI is often extremely impaired, and the management of chronic wounds places an enormous economic burden on the healthcare system.
- Two randomised controlled trials and 12 non-randomised comparative studies reported on a variety of procedures ranging from superficial venous surgery (SVS) and subfascial endoscopic perforator surgery (SEPS) through to deep venous reconstruction (including valvuloplasty, transplantation and transposition) for the treatment of deep venous incompetence. However, deficiencies in reporting, methodological weakness and marked inter-study heterogeneity with respect to patient selection, post-operative management, surgical technique, definition of abnormal venous hemodynamics, symptom grading and diagnostic and venous function testing precluded any definitive synthesis of the data.

- The results of two RCTs and two non-randomised comparative studies suggested that combined SVS/valvuloplasty is a relatively safe procedure that is potentially more effective than SVS alone in preventing ulcer recurrence in patients with primary deep venous incompetence in both the short- and midterm.
- Evidence for the efficacy of valvuloplasty, transplantation and SEPS in the treatment of deep venous incompetence was inconclusive. This was also the case for bypass procedures and iliac stenting in the treatment of deep venous obstruction. The optimal surgery for patients with deep venous obstruction or secondary valvular incompetence remains unclear.
- It is unlikely that a large randomised, or even non-randomised, controlled trial will be conducted to ascertain the safety and efficacy of surgery for deep venous incompetence because the complexity and long-term nature of CVI, plus the small proportion of CVI patients with refractory ulcer, make patient selection and ethical surgical comparison problematic. Well-designed studies with comparable patient groups in each study arm, standardised diagnostic work up of patients and detailed reporting of both hemodynamic results and ulcer recurrence rates would be ideal. However, standardised reporting and collection of data in a registry would also be a move forward.
- Professional bodies such as The Royal College of Physicians and Surgeons of Canada should consider providing guidance, in the form of an evidence based treatment algorithm, that would define when to perform SVS in patients with mixed or deep venous incompetence and what type of deep venous surgery is considered appropriate for different indications.
- While it is important to know whether surgery for deep venous incompetence is efficacious and durable, it is equally important to quantify why less invasive treatments have failed in patients requiring surgery for deep venous incompetence. Given that controversy still surrounds many aspects of CVI, it is clear that further good quality research is urgently needed.

GLOSSARY

Ambulation/Ambulatory - able to work

Angiogenesis - growth of new blood vessels

Anastomose - to surgically unite two hollow tubular structures such as blood vessels

Autogenous - self-generated

Coagulopathy - a defect in the blood clotting mechanism

Cribriform - having numerous small holes

Debride/debridement - removal of dead, infected or foreign material from a wound

Denovo - starting again

Distal - furthest from the point of reference

Edema - presence of abnormally large amounts of fluid in the interspaces of tissues

Endothelialised - covered with the cells that line the cavities of the blood vessels

Epithelium - the covering of the internal and external surfaces of the body

Fascia - fibrous connective tissue of the body

Fibrinolytic - able to cause the dissolution of fibrin

Fistula - an abnormal tube like passage between two internal organs or vessels or leading from an internal organ or vessel to the surface of the body

Hematoma - collection of blood, usually clotted, in an organ, space or tissue

Hemorheologic - pertaining to blood flow

Humoral - proceeding from any body fluid such as blood or lymph

Hypertension - high blood pressure

Hypoplasia - the incomplete development or underdevelopment of an organ or tissue

Interstitial - situated in the interspaces of a tissue

Intussusception - prolapse of one segment of lumen into the lumen of another segment

Leukocyte - white blood cells

Lipodermatosclerosis - characteristic skin changes including fibrosis of skin and subcutaneous tissues, capillary proliferation and fat degradation

Lyse - to break up or disintegrate

Medial - situated toward the midline of the body

Peri - prefix meaning around or near, e.g. perivenous, pericapillary

Phlebitis - inflammation of a vein

Phlebography - a test that is performed by first injecting a radiopaque contrast liquid into a vein and then taking a conventional X-ray

Plethysmography - use of a plethysmograph to register the variations in size or volume of a limb, and hence variations in the amount of blood in the limb

Reticular - resembling a net

Sural - pertaining to the calf of the leg

Subcutaneous - under the skin

Telangiectasia - permanent dilation of groups of capillaries and venules in the skin or mucous membranes

Thrombectomy - procedure to remove a blood clot

Thrombolysis - dissolving of a blood clot

Thrombophlebitis - inflammation of a vein that is associated with a blood clot

Thrombosis - formation, development or presence of a blood clot

Vasa vasorum - nutrient blood vessels which supply the walls of large arteries or veins

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Scope of the Report

This report is a systematic review and critical appraisal of the literature on the various surgical treatments available for deep venous incompetence. Its purpose was to provide information to the Out-of-Country Health Services Committee of Alberta Health and Wellness on the available published evidence regarding the short- and long-term efficacy/effectiveness of these treatments for patients with chronic venous insufficiency, and attendant skin changes/ulceration (CEAP class C4 to C6; see Appendix A), that is refractory to standard care. The report was intended to provide a distillation of the evidence on the current status of surgical techniques for deep venous incompetence in order to inform Health Ministry decisions regarding the reimbursement policy for such surgery within the province of Alberta.

INTRODUCTION

Chronic venous insufficiency (CVI) of the lower limb is a poorly defined term that has been used to encompass venous complaints ranging from minor cosmetic blemishes caused by telangiectasia and uncomplicated varicose veins through to edema, lipodermatosclerosis, and chronic ulceration [1,2].

Symptoms of CVI include sensations of pain (the most frequent complaint), aching, heaviness, leg tiredness, cramps, itching, burning and swelling, restless leg syndrome and pressure in affected calves or legs. Signs include spider veins, reticular or varicose veins, dilation or prominence of superficial veins, skin changes such as pigmentation (the most frequent initial sign), edema, lipodermatosclerosis, eczema and ulceration [3-8].

Pathogenesis of chronic venous insufficiency

The venous system of the lower limb comprises the parallel networks of the superficial venous system, which drains the microcirculation of the skin, and the deep venous system, which drains the muscles and muscular venous sinuses [9,10] (see Figure 1). Short perforator veins that pass through the deep fascia connect these two venous systems. A pressure gradient exists in the venous system such that during relaxation of the calf muscle blood drains from the superficial system into the deep vein network through the greater or lesser saphenous veins, the saphenofemoral and saphenopopliteal junctions, or the perforating veins. Blood may also drain straight into the deep venous system or bypass it entirely by entering the pelvis directly [1,3,10]. Movement of blood up the leg veins toward the heart is achieved via the action of the calf muscle pump and, to a lesser extent, the thigh and foot pumps [1,3]. Valves positioned along the length of the veins prevent the backward flow of blood during muscle relaxation [10]. Normal venous pressure in the superficial system during walking is between 20 and 30 mmHg. Higher venous pressure constitutes venous hypertension and is the main predisposing factor in CVI [3].

Figure 1
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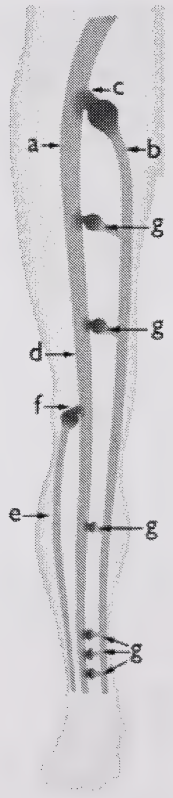

Key
a) femoral vein
b) long saphenous vein
c) saphenofemoral junction
d) popliteal vein
e) short saphenous vein
f) saphenopopliteal junction
g) perforating veins

Venous hypertension in the lower limb can be caused by reflux, venous obstruction or both, while venous pathology can be superficial (the most common), deep or mixed [11]. Venous insufficiency may either be of primary or secondary origin. In primary CVI, abnormalities of the venous wall and the valves, in the absence of previous thrombosis, are the cause of valvular incompetence. Softening of the venous wall, chronic activation in the plasma or a lack of strength in the wall of the vein combined with insufficient support by surrounding tissues can cause venous distension [6, 11]. This has the direct result of preventing the valve leaflets from closing properly across the vein lumen and allowing reflux of venous blood. Valve incompetence may also be caused by defects in the structural integrity of the valve cusps themselves, such as floppy valve cusps, or their detachment from the venous wall. In most cases this is idiopathic but, in rare instances, the defects are congenital [6, 11].

The most common cause of CVI is secondary valvular incompetence and obstruction, either alone or in combination, caused by post-thrombotic damage within the deep veins. In 80% to 95% of patients with venous ulceration, CVI is caused by valvular incompetence, while blockages of the deep veins account for only 3% to 9% of cases[12, 13]. Venous thrombi rarely lyse completely without external intervention. In such cases venous recanalisation is achieved spontaneously in only 50% to 80% of patients after several months [1, 6] and leg ulcers subsequently develop in approximately 5% to 7% of patients after 3 to 7 years [14, 15]. Over that time the residual thrombus undergoes perivenous fibrosis whereby it is impregnated with fibrous tissue and subsequently covered by epithelium, which effectively prevents further lysis of the clot. Endothelialised strands of the residual thrombus can develop a cribriform meshwork across the vein lumen that impedes blood flow, reduces the natural pliancy of the vein, and may irreparably damage valve leaflet function when located near a valve pocket [1, 6]. Other more rare causes of venous hypertension include extramural venous compression, failure of calf muscle pump function, hypoplasia of the femoral or iliac veins and uterine fibroids [11, 16]

Chronic venous hypertension leads to gross venous dilation, vessel elongation and tortuosity with eventual telangiectasia and varicosities [11]. At the cellular level, abnormal metabolism of the connective tissue matrix of the vein wall results in the deposition of pericapillary fibrin, which reduces nutrient flow to the surrounding tissues [6, 11]. Prolonged micro-edema and increased pressure across the vein wall in post-capillary vessels, together with mechanical stress and humoral factors, causes cell activation and production of an inflammatory reaction, resulting in angiogenesis and leukocyte accumulation [11, 17]. This produces skin capillary damage, exudation of proteins into the interstitial space, edema, tissue malnutrition and eventual ulceration [17]. The ulcers tend to manifest in the medial ankle in a single or multiple fashion but may also occur on the side of the ankle or top of the foot [18]. In the worst cases, the ulcers become infected and gangrenous, and may require amputation. Ulcers

of longer than six months duration are also more likely to undergo malignant degeneration [18].

Research continues to unravel the inter-related factors that lead to the tissue degeneration observed in CVI. However, at the cellular level, the exact sequence of events leading to leg ulceration remains elusive, and this has led to controversies in both the evaluation and treatment of patients with CVI.

Classification of chronic venous insufficiency

With the plethora of tests that are now available to aid in the assessment of patients presenting with CVI, it has become necessary to have a comprehensive classification system for quantifying the severity of the disease to facilitate uniform diagnosis. Several classification and scoring systems have been developed, with the two most commonly used being the Widmer (1978) [19] and the Porter classification (1988) [20]. Although these classification systems were popular for many years, their validity was never formally assessed [5].

Advances in knowledge about CVI have stimulated attempts to make a new classification system that comprehensively covers the multifactorial aspects of CVI, while also overcoming the deficiencies in the Widmer and Porter classification systems. Consequently, the CEAP classification was developed by the American Venous Forum in 1994 [21] and is based on Clinical signs, Etiology, Anatomic distribution, and Pathophysiology (Appendix A). It is considered to be the most comprehensive classification to date because it incorporates both clinical information and objective test results, and also clarifies the relationships between contributing factors. However, like its predecessors, the CEAP classification has yet to be formally validated [5, 6].

Epidemiology of chronic venous insufficiency

Prevalence

Chronic venous disease is the seventh most common chronic disease and is estimated to affect up to 2% of the population in Western countries, a prevalence rate similar to that of diabetes [16, 22]. Some type of venous disease is present in approximately 40% of the population between the ages of 30 and 70 years [16, 23].

There are many factors that can confound the epidemiological investigation of ulceration including differing definitions of ulceration and techniques of measurement; differences in the genetic makeup and socio-economical and geographical characteristics of the study group; and inclusion of occupational groups or patients receiving health care who may not be representative of the general population [5, 24]. Ulcer prevalence also tends to be underestimated when data are based on patient self-report or those who voluntarily present for treatment [5]. In addition, ulcers are not always indicative of venous disease but may be due to a co-existing non-venous

musculoskeletal, arterial or neurological pathology [6]. Venous ulcers comprise approximately 54% of all leg ulcers while approximately 3% of foot ulcers are of venous origin [24].

Ulcer prevalence has been estimated at approximately 0.3% of the adult Western population [5, 25]. The prevalence of healed ulcers in the general population is two to four times higher than that of open ulcers, with both conditions affecting between 1% and 1.5% of the population [5, 24, 25]. Ulcers are two to three times more likely to occur in females, compared to males, over all ages. Although the prevalence increases consistently with age in both sexes, chronic leg ulceration is relatively uncommon in people less than 60 years of age [5, 25]. People aged over 70 have a prevalence of between 1% and 4% for chronic venous ulceration [26]. There is a paucity of incidence data for chronic leg ulceration but the annual incidence rate may be in the range of 0.2 and 3.5 per 1000 [5, 25].

Risk Factors

The most important risk factor for CVI is chronic venous hypertension. Several studies have also indicated a link between venous ulcers and prior deep vein thrombosis, even after adjustment for age, gender and other possible risk factors [5, 24]. The prevalence of CVI increases linearly with age [16, 23]. The limited mobility of older patients is likely to be the main cause of this linearity since active patients with a constant degree of venous hypertension do not develop ulcers unless their mobility is reduced [5, 24].

The etiology of chronic venous disease is not well established but there is some suggestion that obesity (in women) and pregnancy may be risk factors [25]. Studies of heredity have suggested a genetic component to the development of CVI, but the results are far from definitive. Many lifestyle factors have also been implicated as risk factors for CVI including prolonged standing or chair sitting, tight undergarments, lack of exercise, hormonal changes, connective tissue laxity, atmospheric pressure, smoking (in men), heavy lifting and constipation [5, 24]. However, none of these factors have been definitively identified as causative.

Ulcer Chronicity

Venous ulceration is a highly chronic condition with about 50%, 20% and 8% of ulcers not healed after 4 months, 2 years and 5 years, respectively. Moreover, estimated recurrence rates range from 6% to 15% [6] with about two thirds of patients experiencing two or more ulcer recurrences [5, 6]. Overall, 25% of ulcers recur within one year [27, 28]. The healing rate of venous ulcers is influenced by a number of factors including the quality and type of treatment offered, follow-up interval, size and duration of the ulcer, patient age and some socio-economic variables [5, 24].

Economic burden of chronic venous insufficiency

CVI has a considerable socioeconomic impact due to its associated morbidity, health care costs and loss of working days [5, 23, 29]. The quality of life of patients suffering CVI is often extremely impaired, and the management of chronic wounds places an enormous economic burden on the healthcare system. For example, venous leg ulceration costs an estimated £400 to £600 million annually in the United Kingdom, with most of the direct costs contributed by dressings and nurse wages [30, 31]. The average cost of care for a single patient with CVI over a lifetime can exceed US$40,000 [18, 31]. In the United States, the estimated annual cost of venous ulcers exceeds US$1 billion. A similar figure represents the total annual cost (direct and indirect) of CVI in both Germany and France [6]. Overall, between 1% and 3% of total health expenditure in many Western countries is spent on the management of venous disorders, which does not include the concomitant social costs such as lost productivity and absenteeism [5, 31, 32]. In the United States alone, approximately two million work days are lost annually because of leg ulcers [33]. While there is no clear indication of the current proportion of Canadians affected by CVI, it is likely that the prevalence rates and resultant economic burden are similar to those of other Western countries. The total healthcare spending for 1999 in Canada was C$89.5 billion while in Alberta it was C$8.6 billion [34]. Therefore, assuming that the proportion of healthcare resources deployed to manage venous disorders is similar to that of other Western countries, it is likely that Canada and Alberta spend, respectively, at least C$895 million and C$86 million annually on the management of venous disease.

Treatment of chronic venous insufficiency

CVI is a complex disease and treatment choices are likely to fail if they are poorly matched to individual patient etiology and disease expression. The four principal treatment modalities for CVI are medication, compression, sclerotherapy and surgery. The traditional treatment of venous ulceration has been non-operative and includes leg elevation, graded compression, wound care and patient education [35],with the ultimate aim of reducing edema, eliminating lipodermatosclerosis and permanently resolving ulceration [3, 5].

Non-surgical treatments for chronic venous insufficiency

Mechanical interventions

Elevation of the legs above heart level for 30 minutes three or four times daily can be effective in reducing edema and improving microcirculation in the skin. However, in more advanced disease this often proves inadequate and compression therapy may be required [3]. Graduated compression therapy is the mainstay of treatment for CVI. It reduces vein calibre and capillary filtration, resulting in reduced venous reflux and edema, increased venous return and improved lymphatic drainage, but the mechanisms

by which this is achieved remain a mystery [3, 5, 18]. Compression is achieved with elastic and non-elastic bandages or stockings, adjustable leggings with interlocking fasteners or, less commonly, intermittent pneumatic compression pumps. Compression therapy is only an effective aid to ulcer healing when a minimum pressure of between 20 and 30 mmHg is exerted at the ankle. It may prove inadequate in patients with massive edema or obesity, and is certainly contraindicated in patients with arterial insufficiency and uncompensated congestive heart failure [3].

Graduated compression therapy is not without its problems. There is some suggestion that those who do not comply with treatment have higher rates of ulcer recurrence than those who do [36]. However, some patients do not have the strength or mobility to pull on the stockings while others find them too hot and uncomfortable to wear, too painful to put on, or too costly to procure. In addition, there is some evidence that inexperienced or inadequately trained nurses apply bandages at widely varying pressures that may not be appropriate for the clinical need [37]. Consequently, standard care is often not achieved, and some patients may look to surgery as a more desirable treatment option for chronic ulceration than long-term compression therapy (personal communication Ms S. DeVries).

Medication and wound care

A multitude of drugs have been used to ease the symptoms of CVI, most commonly as an adjuvant to other therapies. Hemorheologic and venotonic drugs have been used to improve venous tone and lymphatic drainage [5, 18] while other treatments, such as horse chestnut seed extract, hydoxyethylrutosides and, occasionally, diuretics, are administered to reduce edema [3].

Optimal wound care is comprised of debridement, bacterial control and moisture balance [12]. Topical enzymatic debriding agents, growth factors, anabolic steroids, fibrinolytics and other drugs have been used to promote granulation and epithelialisation of the ulcerous wound [3]. The selective use of antibiotics is also employed to try to stem the advent of chronic wound infection. Wound dressing is also an important aspect of conservative management and may include dry or wet non-adherent dressings, occlusive hydrocolloid dressings or zinc-paste-impregnated bandages [3]. The recent development of bioengineered skin substitutes that are absorbed into the wound bed has improved the efficacy of compression therapy when they are used in combination [12].

Sclerotherapy

This ablative technique eliminates incompetent superficial veins by using an injected chemical agent to induce a fibrotic reaction in the wall of the vessel. Sclerotherapy is particularly effective in superficial venous incompetence when there is a large vein located in close proximity to the ulcer. However, surgery is indicated when there is

substantial proximal incompetence in a saphenous vein [26]. Other venoablative procedures currently being explored include radiofrequency ablation and endovenous laser therapy which induce fibrosis by delivering radiofrequency or laser energy directly into the vein, via a catheter, to cause thermal injury of the vessel wall [38].

Surgical treatments for chronic venous insufficiency

The general surgical strategy is to address defects in the superficial and perforating venous systems before considering the deep venous system [39], with the ultimate aim of removing obstruction or venous reflux. Approximately 8% to 10% of patients have recurrent venous ulcers that are refractory to conservative management and, therefore, require surgical treatment [26, 28]. Since approximately 50% of patients with ulceration have only superficial disease, surgical treatment of superficial veins may prove helpful [24]. However, no single operation is applicable to every type of CVI. Consequently, patients with CVI who are potential candidates for surgery must undergo thorough clinical and physiological assessment of arterial and venous systems in order to identify all vascular abnormalities and locate involved venous segments [16, 40]. It is extremely important to distinguish between primary and secondary venous disease when planning surgical intervention because this will affect the type of treatment options available [41].

Surgery for venous obstruction

Bypass procedures

These procedures create an alternate blood flow route by anastomosing a shunt to the incompetent vein and effectively bypassing the occlusion [42]. An adjunctive arteriovenous fistula is often also performed to increase blood flow through the bypass and potentially improve graft patency. Bypass procedures are considered for deep venous obstruction (popliteal vein obstruction or unilateral femoral vein obstruction) and are usually only performed as a last resort [18, 26]. Several types of bypass procedures are available: cross-femoral venous bypass (the most frequently performed reconstruction procedure for chronic obstructive venous disease) [43], saphenopopliteal bypass, femoro-femoral/iliac vein bypass using the saphenous vein, popliteal-femoral vein bypass and saphenous vein crossover bypass (for ileofemoral disease [28]). Veno-venous bypasses and venous grafts are generally used but more recently polytetrafluoroethylene prostheses have also been deployed [26].

Angioplasty

Angioplasty is often used in conjunction with catheter-directed pharmaceutical thrombolysis to treat iliofemoral venous thrombosis and is, therefore, only suitable for patients who have no contraindication to thrombolytic therapy [44]. A balloon-tipped catheter is introduced into the obstructed vein, under ultrasound guidance, and inflated

to open the vessel and improve blood flow. If necessary, a stent is also deployed [18]. Venous thrombectomy is indicated in patients who fail this procedure.

Surgery for venous incompetence

Vein ligation

Vein ligation consists of tying off veins with a suture or wire ligature and is considered to be the optimal treatment for superficial venous disease [28]. For patients with primary CVI and reflux or incompetence in the superficial, deep and perforating systems, ligation of the superficial and perforating veins improves the hemodynamics of the limb [18] by interrupting the transmission of the high pressure in the deep venous to the skin and subcutaneous tissues [16, 18, 26]. Subfascial endoscopic perforator surgery is a newly developed modification of the classic vein ligation procedure (also known as Linton's procedure) whereby endoscopic techniques are used to visualise and ligate the perforating veins [7]. Early results indicate that morbidity and short-term efficacy is potentially better than the conventional procedure [28].

Stab avulsion

This process forcibly extracts the veins through multiple stab holes in the skin using small purpose built crochet hooks. The technique is reserved for CVI caused by reflux in the greater saphenous system and its application is limited to areas above the knee [41, 45].

Saphenous vein stripping

This procedure consists of the dissociation of the superficial from the deep venous system to control venous hypertension caused by reflux or obstruction in the greater saphenous vein [16, 46]. In combination with ligation of the saphenofemoral junction, this is the most common surgical approach for superficial venous insufficiency [38]. The technique uses an intraluminal stripper inserted into the saphenous vein in the opposite direction to normal blood flow. The stripper is then pulled back through the vein toward the insertion point, stripping the vein wall from the surrounding tissues as it passes [45]. Saphenous vein stripping is now most commonly performed from groin to knee in order to avoid saphenous nerve neuralgia.

Valve repair procedures

These procedures are still considered experimental by many surgeons and, as such, are only indicated for patients who have failed all other types of therapy. In fact, some evidence suggests that subfascial ligation should be attempted first since failure rates are high when direct valve reconstruction is performed in the presence of incompetent deep venous perforators [26].

Valvuloplasty

This procedure is likely to be the most appropriate for primary congenital valve failure when reconstruction is considered because it requires the basic valve structure to be intact [26, 28]. A standard groin incision is used to access the most proximal superficial femoral vein valve. Small sutures are then used to either directly plicate the valve cusps (intravenous repair) or to narrow the vein around them so that the valve cusps meet (extravenous repair). External banding valvuloplasty is a new method that places a Dacron-reinforced silicone rubber sleeve around the incompetent vein segment to narrow the vein lumen [45].

Valve transplantation

In this technique for deep venous incompetence, the dysfunctional vein segment in the popliteal or femoral system is excised and replaced with a valve containing segment from a competent axillary or brachial vein (autogenous or cadaveric) [45]. While this procedure works well for patients with severe post-thrombotic syndrome, it can only be used in limbs where complete recanalisation has occurred, otherwise there is an increased risk of thrombosis in the transplanted segment [26].

Valve transposition

This option can be used for both primary and secondary deep venous insufficiency. Vein segment transposition is achieved by anastomosing the incompetent vein to an adjacent normal vein, distal to a functional valve [28]. However, complete competence of the proximal valve in the recipient vein is an absolute requirement for this procedure [26].

Valve reconstruction

Construction of a new valve mechanism has been attempted by placing an external sling around the popliteal vein using either the gracilis tendon or a Silastic sling. Other techniques, such as *in situ* venous valve construction by intussusception [26], denovo valve reconstruction [47] and the use of bioprosthetic venous valves, have also been attempted but they are still experimental.

Skin grafting

Venous ulcers can be excised down to, and including, the fascia and replaced with split-thickness skin grafts. Compression therapy is applied once the graft has taken. Free muscle flap and omentum grafts have also been used in severely diseased limbs [18]. Skin grafting can be performed before, after or at the same time as superficial venous surgery [40].

Current issues in the surgical management of CVI

Surgery for CVI represents an apparent trade-off between a relatively higher incidence of complications and a lower likelihood of symptom recurrence [38], in comparison to less invasive treatments. The complications of venous surgery can include saphenous vein and sural or saphenous nerve damage, wound infection, hematoma and phlebitis [5, 28]. Many authors consider surgery to be merely palliative since the number of recurrences may be decreased but never completely eliminated, particularly when deep venous insufficiency is extant. Thus, controversy still exists regarding the contribution of perforators to venous hypertension [48,49] and the clinical value of surgery for deep venous disease [49]. The surgical strategy for patients with mixed superficial and deep vein incompetence is also under debate [50]. Therefore, it was the aim of this review to assess the efficacy of the surgical procedures used for the treatment of patients with deep venous incompetence, based on a systematic review of the current published evidence, and to determine how this might impact on the surgical choices available to Albertans suffering from the debilitating effects of CVI.

RESULTS

The full methodology for this review is detailed in Appendix B. One hundred and eight studies were identified that potentially met the inclusion criteria of the review. On closer examination of the full text article, 89 of these studies were excluded and the reasons documented (Appendix C). Five potentially relevant foreign language articles were identified. However, these studies were not translated because, based on their English abstract, they did not offer any significantly different or more extensive results than the English language papers. The details of these studies have been tabulated in Appendix C to show the breadth of research available in the non- English literature on this topic. Fourteen papers, comprising two randomised controlled trials (RCTs) and twelve non-randomised comparative studies (Table 2), met the inclusion criteria of the review.

A meta-analysis was not performed because the studies were very heterogeneous with respect to patient selection, outcome measures, adjunctive surgery and the type of surgical procedures used. However, since many studies did not have comparable numbers of patients in each of the study arms, the relative risk (RR) and absolute risk reduction (ARR) plus 95% confidence intervals (CI) were calculated for some outcomes (vein/valve competency or patency rates, absence of reflux, ulcer recurrence rates, improvement in symptoms or clinical status and development of deep vein thrombosis) in order to aid the interpretation of results. Details of the statistical formulae used are presented in Appendix D.

Methodological quality of included studies

Details of the methods used to assess the methodological quality of the included studies, and the results, are outlined in Appendices B and F, respectively.

RCTs

The two included RCTs [50, 51] were of average to poor methodological quality. The studies suffered from deficiencies in reporting and were severely limited by not blinding the study participants or outcome assessors; not indicating whether any attempt was made to conceal treatment allocation; not conducting an intention-to-treat analysis; and not reporting any details of the method of randomisation used. It was impossible to determine the external validity of the two studies because the information provided on the study group and the source population from which they were derived was limited to participation rate only. Thus, it was not clear if any self-selection bias occurred on the part of the patients. There was also insufficient information to determine whether the facility where the patients were treated was representative of the type of hospital that most patients with CVI would attend.

Table 1: Summary of reviewed studies

Study	Level of Evidence	Intervention	No. of Patients	Length of Follow-up	Recruitment Period
Belcaro et al. [51] (1999)	II	SVS	18	10 years	Not stated
		SVS plus valvuloplasty	17		
Makarova et al. [50] (2001)	II	SVS	62	Range 7 to 8 years	1983 to 1984
		SVS plus valvuloplasty	63		
Non-randomised comparative studies					
Jamieson & Chinnick [29] (1997)	III-2	Valvuloplasty	12 limbs	≥ 2 years	1991 to 1992
		Transplantation	4 limbs		
Raju et al. [52] (2002)	III-2	Venous stenting	243 limbs	Mean 9 months	12/1997 to 11/2000
		Venous stenting plus SVS	61 limbs		
Sakuda et al. [53] (2002)	III-2	SVS	14 limbs	Mean 25 months	12/1998 to 02/2001
		SVS plus valvuloplasty	17 limbs		
AbuRahma et al. [54] (1991)	III-3	CFVB	24	Mean 61.2 mths	07/1978 to 06/1988
		SPVB	19	Mean 66.2 mths	
Cheatle & Perrin [55] (1993)	III-3	Valvuloplasty	8	Median 21 mths	Started 1981 but no end date stated
		Transplantation	26	Median 51 mths	
		Transposition	10	Median 46 mths	
		Sling procedure	9	Median 24 mths	
Danza et al. [56] (1991)	III-3	Femoro-femoral bypass	19	Not stated	1968 to 1987
		Transplantation	8		
		Sapheno-popliteal bypass	8		
		Femoro-femoral bypass plus sapheno-popliteal bypass	2		
		Femoro-iliac bypass	3		
		Femoro-axillary bypass	3		

Table 1: Summary of reviewed studies (cont'd)

Study	Level of Evidence	Intervention	No. of Patients	Length of Follow-up	Recruitment Period
Iafrati et al. [57] (1997)	III-3	SEPS SEPS plus SVS SEPS plus valvuloplasty and transposition	9 limbs 4 limbs 1 limb	Mean 6.9 months	12/1994 to 08/1996
Masuda & Kistner [58] (1994)	III-3	Valvuloplasty Transposition Transplantation Valvuloplasty plus transposition	32 limbs 14 limbs 2 limbs 3 limbs	Mean 10.6 years	1968 to 1990
Owens et al. [59] (2000)	III-3	SVS Transplantation	15 limbs 7 limbs	Not stated for the DVI patient group	12/1991 to 09/1999
Perrin [60*] (2000)	III-3	Valvuloplasty Transplantation Transposition Sling procedure	85 limbs 32 limbs 18 limbs 9 limbs	Range 12-96 mths Range 12-124 mths Range 12-168 mths No stated	1988 to 1997 1984 to 1996 1983 to 1997 1988 to 1989
Sottiurai [61] (1991)	III-3	SVS SVS plus valvuloplasty SVS plus transposition SVS plus transplantation	33 limbs 21 limbs 14 limbs 8 limbs	Mean 37 months	09/1981 to 12/1987
Welch et al. [62] (1992)	III-3	Non-angioscopic valvuloplasty Angioscopic valvuloplasty	4 limbs 5 limbs	Mean 32.5 mths Mean 10.6 mths	Not stated

*May include patients from Cheatle & Perrin [55] in its sample

Abbreviations: CFVB – crossover femoral vein sapheno-femoral bypass; DVI - deep venous incompetence; SEPS - Subfascial endoscopic perforator surgery; SPVB – sapheno-popliteal vein bypass; SVS – superficial venous surgery

Follow-up in the two studies extended from seven to ten years, but only one study [51] reported losses to follow-up of greater than 10% in each study arm. Both studies had relatively small sample sizes and were thus underpowered. The potential of confounding in the studies was quite high given that patient withdrawals and dropouts were not factored into the outcome analysis and randomisation may not have been conducted appropriately. Even though Makarova et al. [50] did not report a statistical comparison of preoperative parameters for the two patient groups, they did attempt to control for variations in the clinical dynamics of disease progression in patients beyond just randomisation by stratifying them according to whether they had progressive or stable disease in the five years prior to undergoing surgery. It is expected that this stratification would reduce some of the potential for bias contributed by differences in the degree of CVI extant in the two patient groups.

Non-randomised comparative studies

Three non-randomised comparative studies presented level III-2 evidence, with two being prospective [52, 53] and one retrospective [29]. The remaining nine studies were designated level III-3 evidence because it was unclear whether the comparisons between treatments were concurrent or historical. Two of these studies were prospective [57, 58], two were retrospective [54, 60], and in five studies the method of data collection was unclear [55, 56, 59, 61, 62]. Many of the studies suffered from deficiencies in reporting, which also limited the assessment of their external validity because important details about the patient selection process, participation rate, eligibility rate, and the facility at which the surgery took place were not reported. Follow-up length often varied considerably between treatment groups and this was rarely adjusted for in the final analysis. Many studies had widely disparate sample sizes for the different treatment groups, and all of the included studies were underpowered.

These studies inevitably had the deficiencies inherent to non-randomised studies. Many studies did not specify any patient selection criteria nor did they report preoperative patient characteristics for the individual treatment groups, which made inter-study comparisons problematic. Overall, ten studies failed to conduct a statistical comparison of preoperative patient characteristics for each of the study groups prior to operation. This made it impossible to identify the potential effects of bias and confounding that may have been introduced into these studies by the lack of randomisation of the study participants. In addition, some of the non-randomised studies did not compare similar patients in that they had different levels of disease severity and/or etiology, or were selected for to undergo a particular procedure on the basis of technical feasibility, all of which introduced a strong selection bias. Pre-operative clinical grading of patients was reported by some studies but few used the same classification system, which precluded inter-study comparison. Only six of the non-randomised studies applied inclusion or exclusion criteria to their patients [53-56,

[59, 61], which made the patient populations of the other six studies quite heterogeneous by comparison.

The retrospective non-randomised comparative studies were further weakened by their reliance on the accuracy and completeness of medical records for the veracity of their data. In addition, such retrospective data collection is completely dependent upon the outcome measures noted by the hospital staff at the time, which may not necessarily be adequate for a comparative study. Thus, differences not only in outcomes reported but their method of measurement may result in data mismatch that will affect the validity of any comparative study.

A number of studies were primarily concerned with reporting overall rather than individual results for the various surgical interventions. Therefore, data on efficacy measures for individual treatments were scant and, when available, only quoted for a depleted pool of patients at follow-up. Statistics for post-operative comparisons between the patient groups were also often not reported. The search strategy for this review was date restricted to 1990 onwards to ensure that the included studies reflected the current state of technology for imaging and diagnostic tests. This would ensure that any problems connected with correctly identifying patients eligible for surgery were accurately represented and not biased by earlier problems that have since been resolved by recent technological innovation. However, some of the studies had very long recruitment periods so that the physiological and hemodynamic tests used at the start of the study were superseded before the study was complete; with the result that comparison between pre- and post-operative test values was impossible.

Comprehensive data extraction from the non-randomised comparative studies was hampered by many factors. In some studies it was difficult to discern the raw data values from the graphs presented in the paper because they were displayed in a format that precluded accurate derivation of some of the outcome results. Some studies also had discrepancies between data reported in the text of the paper and those displayed in the tables and graphs, and/or calculation errors in some of the percentage values reported. In addition, the value of the data reported by many articles was severely limited by a paucity of important information regarding patient co-morbidities, surgical methodology and/or statistical information, which often rendered the data uninterpretable. The omission of such key information regarding the surgical population made studies difficult to compare. The outcome measures quoted across the studies were very heterogeneous and many important outcomes, such as ulcer recurrence and presence of reflux, were often not reported. All of these factors, in conjunction with many methodological weaknesses, made the results very difficult to appraise with any confidence. Nonetheless, some of these results can still be used to gain an insight into the possible safety and efficacy issues relating to surgical interventions for patients with deep venous incompetence.

Mean follow-up in the non-randomised comparative studies ranged from nearly seven months to over ten years, with the longest follow-up available on a single patient being 21 years. Because many of the studies pooled the results of the various interventions, follow-up periods for the individual treatment groups were often only provided in terms of a range or a minimum length of time, and in some cases were not available at all.

RCT evidence

Two RCTs [50, 51] had similar selection criteria and only included patients with CVI of primary etiology. Both studies compared a combined superficial venous surgery (SVS) and valvuloplasty procedure with SVS alone. However, Belcaro et al. [51] performed an extravenous valvuloplasty with a no-touch technique that was designed to avoid traumatic vein dissection while Makarova et al. [50] used a more conventional intravenous technique to directly plicate the valve leaflets. In one RCT [50], patients had adjunctive surgery comprising greater saphenous vein stripping and ligation of subfascial perforators. Although the proportion of patients in each study arm that received this additional surgery was similar, it was unclear what contribution these adjunctive procedures made to the final outcomes because only a third of the patients in each study arm received it. The two RCTs differed in their definition of pathological reflux, and Belcaro et al. [51] did not provide any pre- or post-operative clinical grading of their patients, which severely limited inter-study comparison of outcomes. The total number of patients undergoing a combined SVS plus valvuloplasty procedure in the two RCTs was 80. The longest follow-up available on a single patient was ten years.

Efficacy of SVS plus valvuloplasty

Baseline mean ambulatory venous pressure, refill time and saphenous vein diameter were comparable between the two patient groups in Belcaro et al. [51]. Post-operatively, the mean ambulatory venous pressure and refill time were significantly improved in those who underwent SVS plus valvuloplasty, in comparison to SVS. Ten years after surgery, the mean diameter of the saphenous vein was similar to the baseline value in the SVS patients but was significantly reduced in those who underwent valvuloplasty. The mean quality of life score significantly improved in both patient groups with respect to preoperative values, but the degree of change was significantly greater in the valvuloplasty group. At ten years follow-up, colour duplex scanning indicated no superficial femoral vein incompetence in limbs treated with valvuloplasty. In contrast, the patients in the SVS group still had the same level of femoral vein incompetence that they presented with prior to surgery.

Makarova et al. [50] reported that SVS plus valvuloplasty was more successful than SVS in achieving an improvement in clinical class and a reduction in the rate of recurrent varicosities after seven years follow-up. Because the study design incorporated a five

year period of patient observation prior to surgery, it was possible to determine that this difference was mainly due to extremities with the progressive type of clinical dynamics ($p < 0.05$). The results from the patients with the stable type of clinical dynamics were not significantly different ($p > 0.10$) between the two intervention groups. Reflux either persisted at the same level or increased following SVS, whereas over 70% of the patients in the combined treatment group experienced a decrease in reflux and had a competent proximal superficial femoral vein (SFV) valve after seven years follow-up.

Given the variation in outcome measures reported in the two RCTs it was impossible to judge whether the no touch non-occlusive surgical technique of Belcaro et al. [51] provided better results than the standard intravenous valvuloplasty technique used by Makarova et al. [50].

Safety of SVS plus valvuloplasty

Only Belcaro et al. [51] commented on the safety aspects of the procedures. No adverse events, such as superficial or deep vein thrombosis or other complications, were reported for any of the patients in either of the treatment groups over the ten year follow-up period.

Non-randomised comparative study evidence

Valvuloplasty

Four non-randomised comparative studies [29, 55, 58, 60] reported on comparisons of valvuloplasty with other deep vein surgical procedures. It is possible that the results reported in two studies [55, 60] are based on a common core of patients. However, they have been treated as separate studies because of the differing sample sizes and inclusion criteria with respect to CVI etiology (Cheatle and Perrin [55] exclusively included patients with secondary CVI whereas Perrin [60] included patients with Klippel Trenaunay syndrome as well as those with primary, secondary, and mixed primary and secondary CVI).

The majority of the studies [55, 58, 60] used an intravenous valvuloplasty technique. Jamieson and Chinnick [29] were the only authors to exclusively use an extravenous valvuloplasty technique in combination with external banding. The study representing the highest level of evidence [29] was the only study that did not report conducting adjunctive SVS. The other three studies all performed various adjunctive surgical procedures encompassing superficial vein ligation and/or stripping and perforator ligation. This introduced significant confounding to the study results because the additional SVS was not performed uniformly across the individual treatment groups. Consequently, it was impossible to separate the potential contribution to patient outcomes of the deep vein surgery from that of the SVS.

In Jamieson and Chinnick [29], patients were selected to undergo either valvuloplasty or venous transplantation primarily on the basis of descending phlebography and clinical findings. Consequently, the study compared two groups of disparate patients in that the valvuloplasty group had primary insufficiency while the transplantation group had re-canalised deep valve insufficiency. Very few efficacy outcomes were reported for the individual groups, and only a quarter of the limbs underwent post-operative descending phlebography, making these measurements almost useless. There was also no explanation of why so few patients were available for post-operative phlebography. The phlebography results showed that one patient in the transplantation group had major reflux after more than two years follow-up whereas no reflux was evident in the three patients who had phlebography in the valvuloplasty group. However, it is unclear how this related to clinical symptoms and whether the patients were better or worse off with respect to baseline. The overall results from Jamieson and Chinnick [29] showed that the proportion of patients whose symptoms improved or who became asymptomatic post-operatively was similar between the valvuloplasty and transplantation groups. No adverse events occurred in either patient group following surgery.

Masuda and Kistner [58] examined post-operative outcomes after valvuloplasty, vein transposition, transplantation or a combined valvuloplasty and transposition procedure in patients with primary or secondary CVI. Unfortunately, baseline patient information was not reported for the individual treatment groups and, thus, it was impossible to discern whether there was an uneven distribution of possible confounding prognostic factors between the four patient groups.

There was no discernible difference between valvuloplasty and transposition (RR 0.70, 95% CI 0.39 to 1.23; ARR -0.22, 95% CI -0.52 to 0.09) or valvuloplasty/transposition (RR 0.46, 95% CI 0.09 to 2.33; ARR -0.39, 95% CI -0.94 to 0.17) with respect to improvement in clinical status after a mean follow-up of over eight years. However, transplantation (RR 0.23, 95% CI 0.02 to 2.97; ARR -0.72, 95% CI -1.17 to -0.27) patients were 72% less likely to have improved clinical status post-operatively, in comparison to valvuloplasty. There was no apparent difference between transposition (RR 1.02, 95% CI 0.31 to 3.35; ARR 0, 95% CI -0.27 to 0.28) and transplantation (RR 0.71, 95% CI 0.05 to 9.64; ARR -0.23, 95% CI -0.67 to 0.22), in comparison to valvuloplasty, in the likelihood of experiencing severe reflux post-operatively. However, patients were four times more likely to have severe reflux following the valvuloplasty/transposition (RR 4.43, 95% CI 2.31 to 8.50; ARR 0.77, 95% CI 0.42 to 1.13) procedure, in comparison to valvuloplasty. The ten year cumulative success rate was not reported separately for the transposition, transplantation or valvuloplasty/transposition procedures. Nonetheless, the pooled cumulative success rate for these three patient groups, nearly three quarters of which underwent the transposition procedure, was significantly lower in comparison to valvuloplasty. Less than half of the patients had comparable preoperative and post-

operative hemodynamic tests, so data for venous function outcomes was limited to a small subgroup of the patients originally included in the study. Valvuloplasty was associated with the best hemodynamic results and showed significant improvement in both mean fall in ambulatory venous pressure and mean refill time with respect to baseline, as opposed to the transposition procedure in which only refill time improved from its preoperative value. Transplantation and valvuloplasty/transposition showed no improvement in either parameter in comparison to baseline.

Masuda and Kistner [58] also conducted a number of subgroup analyses and found no statistically significant differences in patient outcomes according to duration of pre-operative symptoms, post-operative activity level or duration of follow-up. However, the ten year cumulative success rate of the patients with primary CVI was significantly higher than for the secondary CVI group.

Two studies [55, 60], originating from the same vascular pathology centre, compared patient outcomes following valvuloplasty, transplantation, transposition and the Psathakis sling procedure. Cheatle and Perrin [55] only included patients with evidence of post-thrombotic syndrome that did not have a coagulation disorder. Unfortunately, a statistical comparison of preoperative parameters for the patient groups was not reported, so it was unclear if there was a heterogeneous distribution of such factors as age, gender, history of recurrent ulceration or previous surgery. However, the majority of the included patients had Kistner grade IV reflux. The study was also limited by widely varying follow-up periods which reduced between treatment comparability.

Symptomatic improvement following transplantation (RR 0.71, 95% CI 0.35 to 1.47; ARR -0.19, 95% CI -0.62 to 0.24), transposition (RR 0.94, 95% CI 0.43 to 2.04; ARR -0.04, 95% CI -0.55 to 0.46) or the sling procedure (RR 1.17, 95% CI 0.60 to 2.27; ARR 0.11, 95% CI - 0.35 to 0.58) was not discernibly different from valvuloplasty. The proportion of patients who developed vein/valve obstruction due to thrombosis was similar across the treatment groups and probably reflects their pre-disposition to this type of complication. The likelihood of having a patent vein/valve at the various follow-up periods was similar for transplantation (RR 0.86, 95% CI 0.44 to 1.69; ARR -0.10, 95% CI -0.53 to 0.34) and transposition (RR 1.13, 95% CI 0.56 to 2.25; ARR 0.08, 95% CI -0.40 to 0.57), in comparison to valvuloplasty. However, patients undergoing the sling procedure (RR 0.17, 95% CI 0.02 to 1.15; ARR -0.56, 95% CI -0.99 to -0.13) were less likely to have a patent vein/valve than those undergoing valvuloplasty. Rates of vein/valve competency were also similar with the exception of transplantation patients, who were seven times more likely than valvuloplasty patients to have an incompetent valve at follow-up (RR 0.14, 95% CI 0.03 to 0.60; ARR -0.57, 95% CI -0.97 to -0.17). Ulcer recurrence rates were similar across the different treatment groups, in comparison to valvuloplasty, although the follow-up duration differed substantially (transplantation: RR 0.94, 95% CI 0.16 to 5.44; ARR -0.02, 95% CI -0.60 to 0.56; transposition: RR 1.00, 95%

CI 0.14 to 7.10; ARR 0, 95% CI -0.65 to 0.65; sling procedure: RR 0.86, 95% CI 0.12 to 6.23; ARR -0.05, 95% CI -0.68 to 0.58). The number of patients with recurrent ulcers corresponded closely to the number of patients with vein/valve obstruction, but there was insufficient information reported to confirm whether the same patients had both adverse events. One patient in each of the sling and the transposition treatment groups required re-intervention.

The study by Perrin [60] had a more heterogeneous patient population than Cheatle and Perrin [55]. The procedure undertaken in each patient was largely determined by the feasibility of the technique in the preferred order of valvuloplasty, transposition, transplantation and the Psathakis sling procedure. Consequently, the etiology of CVI varied considerably between each treatment group and the degree of clinical severity (defined by the CEAP classification system) was significantly different between the valvuloplasty, transplantation and transposition groups such that significantly fewer patients undergoing valvuloplasty had healed or active ulceration ($p = 0.01$).

Patients undergoing transplantation were more likely to have reflux at follow-up, in comparison to valvuloplasty (RR 0.42, 95% CI 0.23 to 0.78; ARR -0.36, 95% CI -0.55 to -0.17), whereas transposition had an equivocal result when compared to valvuloplasty (RR 0.95, 95% CI 0.61 to 1.49; ARR -0.03, 95% CI -0.30 to 0.24). Ulcer recurrence rates for transposition (RR 0.97, 95% CI 0.25 to 3.81; ARR -0.01, 95% CI -0.31 to 0.30) and transplantation (RR 1.71, 95% CI 0.77 to 3.79; ARR 0.16, 95% CI -0.08 to 0.41) patients were not discernibly different from those who underwent valvuloplasty. The sling procedure was discontinued after 18 months because none of the patients had hemodynamic improvement. Consequently, very few results were reported for this treatment group. It was unclear how many patients in the sling procedure group had an ulcer prior to surgery. Deep vein thrombosis was more common after transplantation, in comparison to valvuloplasty (RR 2.90, 95% CI 1.42 to 5.89; ARR 0.25, 95% CI 0.06 to 0.43), whereas the rates for the transposition (RR 2.15, 95% CI 0.85 to 5.42; ARR 0.15, 95% CI -0.07 to 0.37) and sling procedure (RR 0.86, 95% CI 0.12 to 5.91; ARR -0.02, 95% CI -0.24 to 0.20) were similar to those of valvuloplasty. Thrombosis was more likely to occur in patients with CVI of secondary etiology than those with a primary cause ($p = 0.003$).

The study by Welch et al. [62] compared the angioscopic valvuloplasty with non-angioscopic valvuloplasty. The study described a progression in surgical method with consequent differences in operative technique and post-operative management between the two patient groups, which in such a small group of patients is likely to result in significant confounding. The non-angioscopic technique involved intravenous valvuloplasty, with half of the patients having the repaired valve segment wrapped with an external polytetrafluoroethylene band. In the angioscopic group, three of the patients had an open operation with venotomy whereas the other two had a closed

operation without venotomy. These two types of surgical approach have the potential to impact quite differently on the durability of the procedure. No separate pre-operative parameters were reported for the two treatment groups, once again making it impossible to ascertain the distribution of potential confounding factors.

Valve patency was achieved in all patients in the angioscopic group as well as the three patients available for post-operative duplex scanning in the non-angioscopic treatment group. All patients had an ulcer at the time of surgery, all of which were healed at follow-up. The two patients in the non-angioscopic valvuloplasty group who received external banding developed deep vein thrombosis but, unlike the other patients in this treatment group, they did not receive anti-coagulant therapy post-operatively. No deep vein thrombosis was reported in patients who underwent the angioscopic technique. There was no significant difference between the two groups in terms of venous refilling time after surgery, nor did the value improve with respect to baseline in either group (only six limbs were measured before surgery while all nine were assessed post-operatively). Unfortunately, post-operative air plethysmography was only conducted in one of the patients who underwent non-angioscopic valvuloplasty so no comparison of these measurements between the treatments could be made. Post-operative duplex scanning was performed in three non-angioscopic valvuloplasty patients and five of the angioscopic valvuloplasty patients. The angioscopic patients had a much shorter valve closure time for both the SFV and popliteal vein, which approached normal values.

SVS plus valvuloplasty

Two studies [53, 61] compared SVS alone with a combined SVS and valvuloplasty procedure. Sottiurai et al. [61] also examined the differences between SVS alone and SVS performed in conjunction with either transposition or transplantation.

The patients included in Sakuda et al. [53] were highly selected in that those with post-thrombotic syndrome, a history of deep vein thrombosis or recurrent veins after stripping were excluded. Allocation to the different treatment groups was determined by patient preference. Consequently, there were more patients with a higher CEAP grading in the combined procedure group, even though all patients had Kistner grade III or IV reflux. The extravenous valvuloplasty was performed with the aid of an angioscope. The proportion of patients who underwent saphenous vein stripping/ligation or perforator ligation during adjunctive SVS was similar between the two treatment groups except for subfascial endoscopic perforator surgery (SEPS), which was performed at least ten times more often in the combined treatment group ($p < 0.001$). However, the number of perforators interrupted was not significantly different between the two groups.

No new ulcers developed after either SVS or combined SVS and valvuloplasty. However, after a mean follow-up of 25 months the valve patency was significantly better after the combined treatment, in comparison to SVS (RR 3.29, 95% CI 1.43 to 7.61;

ARR 0.66, 95% CI 0.39 to 0.92). In addition, significantly fewer patients in the combined group required continued need of elastic support hose. Worsening of pigmentation was reported in 7% of the SVS patients whereas this was not reported as occurring in the SVS/valvuloplasty group. A slight, but not significant, reduction in mean venous volume was reported at one month follow-up in both treatment groups, compared to baseline, but the degree of change observed was significantly greater in the SVS/valvuloplasty patients. A significant improvement in mean venous filling index, compared to baseline, was also registered in both treatment groups after one month, with the degree of improvement being significantly better in the combined treatment group. Similar statistically significant improvements in venous clinical severity score and mean venous disability score were observed in both treatment groups but, once again, these scores were significantly better in the combined group at a mean follow-up of 25 months. The only adverse event reported was a wound infection that developed in one patient in the combined SVS and valvuloplasty treatment group, but this did not prove to be a statistically significant difference.

In Sottiurai et al. [61], the SVS procedure comprised ligation of subfascial perforating veins as well as saphenous vein stripping. Intravenous valvuloplasty was performed in patients with reparable valves otherwise vein transposition or valve transplantation was used. Many of the preoperative demographic and prognostic parameters were only reported for the combined patient group, so it was unclear what the distribution of potential confounding factors was. However, while venous incompetence in the SVS group was clearly not as extensive as in the other three treatment groups, all of the patients included in the study presented with recurrent leg ulcers. The post-operative outcomes reported for the each of the intervention groups were limited. Comparable rates of valve competency were achieved in all three combined procedures between one week and three months follow-up. After a mean follow-up period of 37 months, ulcer recurrence rates in patients treated with SVS plus valvuloplasty (RR 0.33, 95% CI 0.13 to 0.84; ARR -0.39, 95% CI -0.62 to -0.15) or SVS plus transposition (RR 0.37, 95% CI 0.13 to 1.06; ARR -0.36, 95% CI -0.63 to -0.09) were lower than those reported for the SVS group. The results for transplantation (RR 0.43, 95% CI 0.13 to 1.49; ARR -0.33, 95% CI -0.67 to 0.02) showed a strong, but not significant, trend toward a lower rate of post-operative ulcer recurrence for the combined procedure, in comparison to SVS. When the SVS rate of ulcer recurrence was compared to the pooled rate for all three SVS plus valve correction procedures, the latter value proved to be significantly lower ($p < 0.001$). This was also true for SVS versus the pooled results for the combined procedures with respect to post-operative transvenous pressure ($p < 0.005$). Three times more patients in the SVS group were in continued need of post-operative external support at the end of the study period, in comparison to the other three treatment groups ($p < 0.001$).

Although the results from the two RCTs [50, 51] comparing SVS with a combined SVS and valvuloplasty procedure reported on different patient populations and outcomes, the

limited results from these two non-randomised comparative studies seem to indicate a general trend of an increased benefit for patients with deep venous incompetence following a combined SVS and valvuloplasty procedure, in comparison to a SVS procedure alone.

SVS versus transplantation

Owens et al. [59] compared SVS with transplantation in patients with CVI. However, since the focus of this paper was on the effectiveness of air plethysmography in predicting clinical outcome rather than on the effectiveness of the surgical procedures themselves, few relevant outcomes were reported. In addition, only data from a small proportion of the patients actually included in the study could be tabulated because the majority of the limbs operated on had only superficial CVI with no deep vein involvement. The etiology of the patient groups was dissimilar in that those undergoing SVS had primary CVI whereas the transplantation group had secondary CVI exclusively. Unfortunately, the length of the follow-up period for the small patient subgroup with deep venous incompetence could not be determined from the information available in the paper, which seriously undermined the value of this data for assessing treatment efficacy. Nevertheless, the very limited data suggested that while both procedures produced a similar degree of reduction in the venous filling index, this parameter did not normalise in the patients who underwent transplantation whereas it reached normal values in eight of the fifteen patients in the SVS group.

Subfascial endoscopic perforator surgery (SEPS)

Iafrati et al. [57] presented their early results of SEPS in 18 limbs as a case series study. However, this study met the inclusion criteria for the review because raw data for some of the post-operative outcomes were reported for all of the 18 limbs included in the study, making it possible to compare results between the procedures in a secondary analysis. This study was tabulated as a prospective non-randomised comparative study (level III-3 evidence) (Table 2) because it was unclear whether the treatment comparisons were concurrent or historical.

A secondary analysis of comparisons between SEPS alone or in combination with either SVS or valvuloplasty and transposition was performed. However, the sample sizes were disparate and patients were not equally distributed with respect to many of the preoperative parameters. The SEPS patients had mixed primary and secondary etiology whereas the other two treatment groups had secondary causation exclusively. The anatomical distribution of incompetence also differed between the patient groups, and it is likely that factors such as this determined the type of procedure that was performed in each patient. However, clinical severity was similar in that over 75% of the patients included in the study presented with active ulceration while the remainder had healed ulcers. Both of the combined surgical procedures had similar outcomes, in comparison to SEPS performed alone, in terms of symptomatic improvement (SEPS

plus SVS: RR 0.75, 95% CI 0.25 to 2.22; ARR -0.17, 95% CI -0.75 to 0.41; SEPS plus valvuloplasty and transposition: RR 1.50, 95% CI 0.95 to 2.38; ARR 0.33, 95% CI -0.34 to 1.00). Reported adverse events included deep vein thrombosis, transient neuropathy in the medial calf and minor wound infections but it could not be determined which of the individual treatment groups these patients belonged to.

Bypass procedures

Two studies [54, 56] compared different types of venous bypass procedures in patients with deep venous obstruction. AbuRahma et al. [54] assessed crossover femoral vein sapheno-femoral bypass versus sapheno-popliteal vein bypass while Danza et al. [56] compared five different bypass procedures for various functional vein obstructions. In the latter study, a small group of the patients who presented with iliac vein thrombosis underwent a saphenous vein transplant rather than venous bypass.

Pre-operative parameters such as clinical grade, age and gender mix appeared to be evenly distributed between the two treatment groups in AbuRahma et al. [54], though this was not confirmed statistically. However, the treatment specific surgical inclusion criteria applied to each patient group effectively meant that patients were not eligible for both operations. Thus, individual anatomic considerations for each patient dictated which type of bypass was performed. There appeared to be little difference between crossover femoral vein sapheno-femoro bypass (CFVB) and sapheno-popliteal bypass (SPVB) with respect to improvement in clinical status; change in mean venous refill time; change in mean maximum venous outflow; and need for re-intervention after a mean of 61 and 66 months follow-up, respectively. The proportion of patients registering abnormal strain gauge plethysmography results after a minimum of one year follow-up was also similar between the two treatment groups. The crude graft patency and cumulative patency rates for CFVB, compared to SPVB, were equivocal. No mortality was reported within 30 days after surgery in either patient group, and the rate of deep vein thrombosis development was similar. One patient in the SPVB group had a post-operative wound infection but this was not reported in the CFVB group.

Danza et al. [56] provided little information with respect to the clinical grading, age, gender mix and other preoperative parameters of the included patients. The only outcome data available for the individual treatment groups was a subjective description of patient outcome as excellent (asymptomatic), good (markedly improved symptoms but with persisting edema) or poor (no improvement). In patients treated for iliac vein thrombosis, saphenous vein transplant achieved a similar rate of symptomatic improvement as free femoro-femoral bypass (RR 0.59, 95% CI 0.23 to 1.55; ARR -0.26, 95% CI -0.66 to 0.14). All patients who underwent femoro-iliac bypass were asymptomatic post-operatively, but thrombosis in these patients was caused by an iatrogenic ligature of the common femoral vein that had occurred during their infancy. Thus, it is unlikely that these patients would have developed venous insufficiency

without the intervention that caused the venous obstruction in childhood and, therefore, their post-operative recovery would not be complicated by any inherent coagulopathy or venous system defects. The proportion of patients who were asymptomatic after undergoing sapheno-popliteal bypass was similar to those who achieved this after free femoro-femoral bypass. However, the former patients were operated on for SFV thrombosis while the latter presented with iliac vein thrombosis. None of the patients who were treated with femoro-axillary bypass or femoro-femoral graft plus sapheno-popliteal bypass were free of symptoms post-operatively. Post-operative phlebograms were obtained in 30 of the 43 patients. Eight thrombosed bypasses were found but it was not possible to determine which treatment groups these patients belonged to.

Iliac stenting

One prospective non-randomised comparative study [52] examined the effects of iliac venous stenting alone or in combination with SVS in patients with CVI caused by narrowing of the iliac vein. Unfortunately, the sample sizes of the two treatment groups were very uneven and the study did not report what factors determined which of the two surgical treatments the patients would receive. Despite demarcating the venous stenting plus SVS patients as a separate subgroup for comparison in the paper, the majority of the preoperative variables and post-operative outcomes were only quoted for the entire patient pool. Thus, it was unclear what the distribution of prognostic and other confounding factors may have been between the two patient groups.

Just over a fifth of all the patients included in the study presented with healed or active ulceration. However, there was no significant difference between the two treatment groups in terms of post-operative ulcer recurrence after a mean follow-up period of nine months (RR 0.84, 95% CI 0.45 to 1.57; ARR -0.09, 95% CI -0.42 to 0.23). Similar improvements in swelling, pain and ulcer healing were observed in both patient groups, and this was independent of whether or not an ulcer was present at surgery [52].

Discussion

Limitations of the review

There is always a danger in attempting to synthesise a collection of poor evidence into a meaningful whole. The included studies were assessed using a quality tool with the expectation that this would aid in identifying which studies should be given more weight in the overall synthesis. Unfortunately, because there were so few studies on any one surgical procedure, and all of them had such major design flaws, the original aim of the quality assessment became redundant. However, it was not without value because it provided a framework for highlighting the major study design and execution flaws.

Many of the included studies had substantially different sample sizes between the treatment groups, so a measure of association (ARR and RR) was calculated to avoid the biased interpretation that may occur from directly comparing only the proportion of patients in each group that had a particular outcome. Even though these measures were not pooled, this approach could still be criticised because it forces a comparison between treatments that may not be appropriate given the heterogeneity of some of the patient groups, and may be misleading. For this reason, a measure of association was not calculated for studies such as Jamieson and Chinnick [29], which compared the use of valvuloplasty in patients with primary insufficiency against transplantation performed in patients with secondary insufficiency. However, ARR's and RR's were calculated for studies where the patients groups were less disparate.

Safety and efficacy of surgery for deep venous incompetence

Good studies are defined by rigid inclusion criteria, extensive evaluation, highly standardised treatment, validated and clinically relevant outcomes, a lengthy follow-up period and impartial investigators [63, 64]. All of the studies available for review failed in at least one of these requirements. Therefore, the poor evidence quality, small sample size and limited data reporting in the majority of the studies meant that only very general conclusions could be drawn from the data.

RCT evidence

The two included RCTs lacked much detail regarding study design and patient selection, which precluded an accurate assessment of their overall quality. Consequently, their study quality could only be rated, at best, as poor to average. Unfortunately, neither RCT reported the rate of ulcer recurrence. In addition, the studies largely focused on hemodynamic outcomes, which do not necessarily correlate with clinical improvement in patients [29, 55]. The patient population in both studies was similar in that they exclusively had primary deep venous insufficiency of mild to

moderate severity (CEAP class C4 or lower) with no prior ulcer recurrence. However, this was a highly selected patient group since most patients considered eligible for deep vein surgery usually have more severe symptoms (CEAP class C5 to C6) [53] with a predominantly secondary disease etiology [12, 13].

Overall, patients who underwent the combined SVS and valvuloplasty procedure had a greater improvement in post-operative hemodynamic outcomes than those in the SVS treatment group. Makarova et al. [50] demonstrated that this improvement in their study was largely due to the benefit derived by patients in the study with the progressive type of clinical dynamics (propensity to increase in clinical class over time in the absence of intervention). Patients with more stable clinical dynamics that were less prone to deterioration had similar outcomes regardless of the type of treatment they received. The limited evidence from one RCT [51] suggested that both SVS and combined SVS/valvuloplasty were safe.

The Bottom-line: Limited evidence suggested that combined SVS/valvuloplasty is a relatively safe procedure that is potentially more effective than SVS in preventing ulcer recurrence in patients with primary venous insufficiency in both the short- and mid-term.

Non-randomised comparative evidence

Many of the non-randomised comparative studies were lacking in essential data, such as patient co-morbidities and severity of preoperative symptoms, and had very subjective inclusion criteria, if any at all. The multiple comparisons, uneven sample sizes, heterogeneous patient populations and few common outcomes of the non-randomised comparative studies precluded any inter-study comparisons that may have aided the synthesis of evidence. Only six of the fourteen included studies reported ulcer recurrence rates.

Valvuloplasty (in patients with primary etiology) and transplantation (in patients with secondary etiology) achieved similar degrees of symptomatic improvement with no adverse events [29]. Transplantation and combined valvuloplasty/transposition were inferior to valvuloplasty with respect to improvement in clinical status and reflux, respectively, whereas transposition was not discernibly different from valvuloplasty in patients with primary or secondary CVI [58]. One study [55] found that symptomatic improvement and ulcer recurrence rates were similar for transplantation, transposition and the Psathakis sling procedure, in comparison to valvuloplasty, in patients with secondary CVI. However, transplantation and the sling procedure resulted in lower vein/valve competency and patency, respectively, compared to valvuloplasty. Another study [60] looked at the same procedures in a more heterogeneous patient population and found similar ulcer recurrence rates for the surgical techniques, but transplantation had poorer outcomes with respect to reflux and deep vein thrombosis, in comparison to valvuloplasty. However, there were more patients with secondary CVI in this

treatment group compared to either the valvuloplasty or transposition groups, which may have affected the results. It was not possible to attribute the positive effects on patient outcomes solely to the deep vein surgery in these studies because all, bar one [29], employed adjunctive SVS. In addition, all of the studies employed some kind of post-operative management regimen involving compression therapy and it was unclear what impact this may have had on patient outcomes.

Angioscopic valvuloplasty appeared to be as safe as non-angioscopic valvuloplasty in the small study [62] that reported this procedure, but the data were too sketchy to derive any definitive synthesis of the efficacy data.

SVS plus valvuloplasty proved to be superior to SVS alone in patients with primary CVI with respect to improvements in clinical and hemodynamic parameters [53]. Sottiurai et al. [61] also found that SVS combined with valvuloplasty, transposition or transplantation provided better vein/valve competency and ulcer recurrence rates than SVS. However, the disease etiology of the study population was not reported. These trends in favour of the combined SVS/valvuloplasty procedure, in comparison to SVS, agreed with the RCT results. In contrast, the symptomatic improvement achieved after SEPS was the same as that for SEPS in combination with SVS or valvuloplasty/transposition [57]. The very limited hemodynamic data on SVS versus transplantation suggested equivocal results [59].

The Bottom-line: Evidence for the efficacy of valvuloplasty, transplantation and SEPS in the treatment of deep venous insufficiency was inconclusive. The optimal surgery for patients with secondary disease remains unclear.

Safety and efficacy of surgery for deep venous obstruction

Non-randomised comparative evidence

The symptomatic improvement achieved after iliac venous stenting alone was the same as that for stenting performed in combination with SVS [52]. In contrast, bypass procedures seemed to show mixed results and were difficult to decipher given that very specific anatomical requirements dictate which procedure is performed. This means that, generally, the patients in one treatment group are ineligible to undergo the alternative bypass procedure for technical reasons. Thus, the comparative treatment populations do not represent a common patient pool but rather a highly selected and mutually exclusive one.

The Bottom-line: Evidence for the efficacy of bypass procedures and iliac stenting in the treatment of deep venous obstruction was inconclusive. The optimal surgery for patients with venous obstruction remains unclear.

Further considerations

Patient selection for CVI surgery

Contraindications for CVI surgery include peripheral arterial disease, recent thrombophlebitis of the deep veins, coagulopathy, pregnancy and significant co-morbidity [55, 65]. However, the lack of applied exclusion criteria for the majority of the reviewed studies meant that it was not possible to derive from these any definitive conclusions regarding the possible contraindications for the various surgical procedures.

The complexity of CVI and the mutual exclusivity of some surgical treatments make rigorous patient selection for deep vein surgery essential. Because of the variation in vein morphology between primary and secondary disease, different surgical approaches must be used to treat them. Internal valvuloplasty is often considered the gold standard procedure for treating the normal but dysfunctional valves seen in primary disease, but it is of no value in patients with the distorted valves and thickened vein walls of secondary disease except as an aid in maintaining or restoring competence after valve transposition or transplantation procedures [66-68]. Therefore, a thorough diagnosis must encompass not only the structural and functional abnormalities in the venous system but also the cause and extent of reflux and/or obstruction in the superficial, perforator and deep veins [66].

The surgical procedure for each patient must be completely individualised [67, 69]. Clinical examination, on its own, is inadequate to provide the information required for a full diagnostic work up of patients with deep venous insufficiency. Clinical assessment can vary both within and between observers with an intra-observer agreement of only 30% and an inter-observer agreement of 60% in evaluation of post-operative visual improvement of symptoms [70]. The development of more objective measures of venous function, such as duplex ultrasound scanning, over the past decade has markedly improved diagnostic capabilities and knowledge of venous hemodynamics, which in turn has improved the surgeon's ability to select the appropriate surgical treatment for each patient [71, 72]. Diagnostic imaging is also important in determining both the location and extent of the surgery required.

The rationale for deep vein surgery is to remove obstruction and correct reflux, thereby restoring one way blood flow within the leg veins [66, 73]. Surgery should only be undertaken based on the need to relieve debilitating symptoms, such as lipodermatosclerosis or ulcer, rather than on vascular laboratory findings because many patients with clinically demonstrated valvular incompetence remain asymptomatic over long periods of time [50, 67, 69]. It is clearly not appropriate to expose such patients to the potential dangers of invasive vein surgery when they are not sufficiently symptomatic to warrant it. The counter argument suggests that deep vein surgery should be considered early in the management of selected patients because patients with severe

CVI often exhibit pronounced atrophy and necrosis in the calf muscle cells, to the extent that even valve repair will not reverse the deterioration [74]. However, for this to be an effective treatment plan, given the potential morbidity of surgery, it must be possible to determine not only the optimal time for treatment in the course of disease progression but also to identify those patients with the particular clinical and hemodynamic characteristics who would receive the most benefit [74].

This problem is inextricably linked to the additional need of defining the anatomic and hemodynamic criteria that may identify those patients who are at high risk of ulcer recurrence and who are likely to fail conservative non-operative treatment [75]. These patients would be prime candidates for early surgical intervention. It is already known that patients with post-thrombotic syndrome are more likely to suffer ulcer recurrence following conservative treatment than those with primary valvular incompetence [75,76]. Other predisposing factors include increased venous volume and venous filling index, a recurrence of pain and presence of deep venous disease [75]. The long-term and generally progressive nature of CVI makes the expense and inconvenience of protracted conservative therapy impractical for treating refractory ulcers. It would be valuable to improve the risk-benefit ratio of surgery by being able to select the patients that would benefit from such treatment and have it performed earlier in the course of the disease than it is at present [57]. However, the cost of invasive surgical therapy would have to be balanced against the comparatively low but recurrent and ongoing cumulative costs of long-term medication, supplies and personnel time used in conventional therapy [52].

Technical considerations

Deep vein reconstruction procedures are highly operator dependent, requiring meticulous technique and considerable skill [62,68]. Because the surgical approach and technique used is often different in each patient, the operative experience of the surgeon can be an important factor given the many intra-operative decisions that have to be made during the operation. For example, in the case of valvuloplasty, a surgeon's knowledge and experience would impact on which valves were repaired, what type of venotomy was used to expose the valve leaflets, and the number and location of the sutures required to make the valve competent [62]. This is reflected in the fact that operations performed by surgical trainees and staff grade surgeons result in persisting venous incompetence in 41% of patients, compared with 6% for consultants [77]. In addition, a thorough knowledge of venous morphology and potential drainage pathways is essential given the variation in anatomy that can occur with respect to the number and position of veins, vein tributaries and vein valves [78].

It is self-evident that there is likely to be a lower rate of operative success while the surgeon is on the learning curve. This could be largely avoided by a rigorous training period during surgical residency that absorbed the learning curve. However, this may be difficult to implement given the low volume of the procedures requiring this kind of

intensive training. Nonetheless, since approximately 20% of varicose vein surgery is performed for recurrence, the majority of which is due to inadequate or inappropriate surgery [79,80], a review of current surgical techniques and surgeon training may be necessary in order to reduce the high rate of re-operation following leg vein surgery.

There are a number of methods currently used to assess the viability of a repaired valve or transplanted venous segment intra-operatively. These techniques include intra-operative Doppler assessment with Valsalva or thigh compression, the strip test, or irrigation of the repaired valve under angioscopic visualisation [62]. While the studies included in this review could not confirm whether the addition of intra-operative testing improved patient outcomes, it seems likely that it would. There are, however, limitations in these operative testing techniques because the amount of venous pressure that can be created intra-operatively in the anesthetised supine patient does not correspond to the higher pressures generated when a standing patient performs the required leg manoeuvres [73]. In addition, routine vein dissection can cause venospasm, which makes the repaired valve seem more competent at the time of operation than it is when the vein wall is relaxed, and this can result in inadequate surgical repair of the valve [73,81].

Diagnostic testing is essential for ascertaining etiology, localising the surgical site and determining the extent of disease [3]. However, the diagnostic and hemodynamic tests used to clinically assess patients with CVI are fraught with technical difficulties. Some tests provide information on venous anatomy while others quantify venous function; some provide qualitative information while others are more quantitative. Thus, there is no one test that can serve as a universal reference, and many tests, while considered useful, have not been formally validated [5]. This has been further complicated by the advent of less invasive diagnostic tests, such as continuous wave Doppler ultrasound and duplex Doppler ultrasonography, which were developed in an attempt to overcome the invasiveness, cost and often significant morbidity associated with ascending phlebography [3,6]. Consequently, diagnostic tests have not been used uniformly, which has led to the recent publication of consensus documents in an attempt to clarify the bewildering choice of tests available [5,6]. However, controversy over which test to use still remains because of the fact that the current popular ultrasonographic imaging methods are extremely operator dependent and can be problematic in patients with obesity, swollen legs or when imaging above the inguinal ligament is required [6]. Diagnosis using other more conventional tests can be further complicated by the presence of edema, lipodermatosclerosis and ulcer [60], which can hinder patients from successfully performing the leg manoeuvres required to obtain accurate test results.

It has been stated that surgical or medical management of CVI can only be palliative [26], and that there is a limited role for surgery in CVI [3]. But the advent of less invasive

alternative techniques for patients with deep venous incompetence, such as iliac stenting, no-touch vein dissection and angioscopic valvuloplasty, promise a shorter hospital stay and recuperative time, higher patency rate and lower morbidity. However, even these procedures still require a degree of expertise that is not currently available on a large scale [52]. Thus, the surgical options for treating patients with CVI are continually evolving, which gives more options to the surgeon for tailoring the operative technique to the needs of the individual patient.

It is currently unclear from the published evidence where all of the current surgical options for correcting deep venous insufficiency may be situated in the armamentarium of the vascular surgeon, but it is clear that most of the techniques represent complementary points on a continuum of treatment rather than competing procedural choices. Patient selection and surgical experience still appear to be pivotal in the overall success of surgery in patients with deep venous insufficiency, and this may have ramifications for the education and accreditation of surgeons in these procedures.

Clinical practice guidelines

Numerous guidelines have been published documenting the prescribed treatment algorithm for CVI. Quite detailed recommendations exist for patients with superficial venous disease, but the dearth of evidence for the treatment of deep vein incompetence is reflected in the universal advice that while compression is generally advised, no other treatment has been shown to be effective. This pronouncement is in line with the results obtained from this review.

A consensus document produced at a meeting in 1997 under the auspices of the American Venous Forum, the Cardiovascular Disease Educational and Research Trust, the European Society of Vascular Surgery, the International Angiology Scientific Activity Congress Organization, the International Union of Angiology, and the Union Internationale de Phlebologie [6] stated that one surgical intervention can not be recommended over another and highlighted the importance of considering long-term outcomes from RCTs that compare existing therapies for all categories of CVI.

An evidence based report by the Venous Insufficiency Epidemiologic and Economic Studies Task Force [5], which reviewed all available publications on chronic venous disease of the leg from 1983 to 1997, recommended that compression should be the main treatment in patients with active ulcer and superficial venous incompetence, and that this can be supplemented by sclerotherapy or SVS provided that no deep vein incompetence was present. There was no evidence that surgical treatment of superficial venous insufficiency, in the presence of deep vein incompetence, prevents ulcer recurrence or that surgical treatment for active ulceration, following deep vein thrombosis or in the absence of reflux, was effective.

It is unlikely that a large randomised, or even non-randomised, controlled trial will be conducted to answer the question of safety and efficacy of surgery for deep venous incompetence. However, standardised reporting and collection of data in a registry would be a move forward. In addition, professional bodies such as The Royal College of Physicians and Surgeons of Canada should consider providing guidance, in the form of an evidence based treatment algorithm, that would define when to perform SVS in patients with mixed or deep venous incompetence and what type of deep venous surgery is considered appropriate for different indications.

Future research

Some of the potential confounding factors in the study of surgery for deep venous incompetence are almost impossible to control. One consideration is that the surgical procedures are evolving over time such that an analysis of the evidence can only provide a snapshot of the situation at the time the assessment is done. This is also true for the continuous advances being made in diagnostic technology that can have a significant impact on surgical practice, not only via the identification and quantification of disease in patients but also through furthering the understanding of the disease process itself.

Nevertheless, there are many confounding factors that can be controlled for, or at least mitigated. A prospective blinded randomised controlled trial is considered the most scientifically rigorous method of evaluating a new surgical therapy [82]. However, such study designs are often not applicable, feasible or even ethical to undertake in surgical practice. As the current data suggests, concurrently controlled trials are a rare occurrence in the area of deep vein surgery. One of the main prohibitive factors is the relatively small number of patients whose symptoms are refractory to conservative treatment and SVS, and the even smaller patient subgroup who would actually be eligible to undergo more invasive treatment. For example, in the one study [50] that applied limited exclusion criteria to their study population and provided some documentation of the patient selection process, only 8.9% of the initial small pool of patients presenting with primary CVI were eligible to undergo valvuloplasty. Thus, an adequately sized RCT or non-randomised comparative study, in which the different treatment populations were truly comparable, could only be achieved via a multicentre trial design. This is further hampered by the small volume and highly specialised nature of these surgical techniques, which has meant that they are largely confined to specialist vascular centres [52].

The variety of underlying causes of CVI can also limit the study population. For a controlled study to be meaningful, the patient population needs to be stratified in terms of their presenting indications, severity of disease and diagnosis. Many studies were excluded from this review because the results for the patients suffering from deep or mixed venous incompetence were combined with those of patients presenting with

isolated superficial or perforator incompetence; or because results for patients with primary disease were pooled with those of patients with secondary etiology. This inappropriate pooling of data renders it meaningless because factors such as the presence of deep vein incompetence and secondary disease are potential prognostic factors in CVI surgery outcomes.

Furthermore, Makarova et al. [50] have demonstrated that study results can be skewed by the uneven distribution of patients with different clinical dynamics among the treatment groups. For example, patients with the progressive type of clinical dynamics (associated with SFV reflux, increasing greater saphenous vein reflux and progressive deterioration in clinical class) had significantly lower improvement rates following combined SVS/valvuloplasty, compared to those with the stable type (no change in clinical status over time in the absence of surgery). Therefore, the efficacy of a procedure could be exaggerated if there were more patients with stable clinical dynamics in the one treatment group, compared to the others. A corollary to this is the possibility of underestimating the difference between treatments if patients of one clinical type show similar rates of improvement regardless of treatment, as was observed by Makarova et al. [50] in patients with the stable type of clinical dynamics.

It is not surprising that there is continuing controversy regarding the value of deep venous surgery given the between study, and even intra-study, variation in case mix and selection criteria. A continuing problem is that many of the non-randomised comparative studies do not recruit comparable patient groups for each study arm. It is useless to compare different surgical techniques when the patients in one treatment group are precluded by their anatomy or disease state from undergoing the comparative treatment. This is particularly true when valvuloplasty performed in patients with primary etiology is compared with a different surgical technique exclusively performed in patients with secondary causation. This inappropriate comparison between the two mismatched patient groups adds a confounding factor to operative outcomes and introduces a strong bias in favour of valvuloplasty because patients with primary etiology are likely to present less technical difficulty for the surgeon, while secondary CVI is a predisposing factor for a negative operative outcome [76].

It is also often the case that the patients with the higher clinical scores undergo the more invasive operations. This can bias the safety outcomes in favour of the surgery performed in patients with milder symptoms. In addition, it is likely that the latter patients fare better because they have less co-morbidity and greater mobility, both before and after surgery. While this probably reflects the selection process that commonly occurs in clinical practice, it does little to further the scientific assessment of the safety and efficacy of these procedures. It is also unclear whether including patients that received treatment for both legs may be a confounding factor. It is possible that the

extra pain incurred from bilateral surgery causes patients to be less mobile and heal more slowly, thereby causing a bias in favour of the treatment group that included fewer bilateral operations.

Many of the included studies employed adjunctive SVS in an ad hoc manner in the treatment groups, and generally not in all patients within a study arm. Therefore, it was impossible to ascribe effect to either procedure individually or collectively. This was further complicated by the many and varied post-operative management regimens that were employed. While these were generally applied uniformly to all of the patients included in the study, it was never noted what degree of compliance was achieved and whether this differed between the treatment groups. This made it impossible to ascertain the extent to which the post-operative management program contributed to patient outcomes. It would be helpful in future research to quantify this by comparing patients who have undergone the same surgical procedure but had either different post-operative care or none at all. A measure of the level of compliance achieved with the post-operative care regimen is essential.

Intention-to-treat was never stated in any of the studies, though some authors conducted an intention-to-treat analysis by default when there were no losses to follow-up. When there were dropouts or withdrawals, the reason was usually not given or was too vague to be meaningful. Some studies only conducted post-operative follow-up on a subset of the patients initially treated. This is most likely due to the difficulty in justifying the expense and potential risk of morbidity (particularly for invasive tests like phlebography) of conducting further clinical tests in an asymptomatic patient following successful surgery and/or being able to entice such a patient back for follow-up examination. Another problem is that because of the long follow-up period required to document changes in the clinical status of CVI patients, dramatic changes in diagnostic technology tend to occur in the interim. Consequently, it was sometimes the case that the venous function data collected preoperatively in a study could not be compared to the post-operative data collected in the same patient because a different physiological test was used, making baseline and post-treatment comparisons impossible. This added considerable bias to the outcome data, particularly given that those patients with shorter follow-up who were more likely to be reported in the study results were operated on much later in the study period. These patients are likely to display better outcomes than those patients treated earlier in the study because of the shorter follow-up time and also the advantage of being operated on after the effects of the learning curve have dissipated.

To date, the value of the results reported in many studies have also been limited because the objective measures of symptom improvement, such as venous function results, were often not uniformly applied, making intra- and inter-study comparison problematic. The comparability of examination results after CVI surgery is also often

compromised by the different inclusion criteria and examination methods used, as well as the lack of standardised well-defined operative outcomes. This was evident in the current series of data in which many studies did not report ulcer recurrence rate or ulcer free interval, which are generally considered to be the ideal objective measures of treatment success in surgery for deep venous insufficiency [39, 55, 76]. Measures such as deep vein thrombosis occurrence and reflux are often defined differently between studies and are dependent on both the measurement methods used to identify them and the timing of their application. In addition, rates of deep vein thrombosis do not necessarily correlate with rates of vein/valve obstruction, particularly if the thrombosis occurs at a distance from the operative site [60]. The formal validation and universal adoption of the CEAP classification system for reporting patient outcomes would also improve inter-study comparisons.

In recognition of the tendency for initially favourable results to deteriorate with time, it has been suggested that a minimum period of six months follow-up is required for documenting clinical outcome following CVI surgery [83]. It is also considered that, given the long-term nature of CVI, follow-up for at least five years is necessary to ascertain procedure durability [57]. Needless to say, many of the included studies did not meet this minimum follow-up length while others manifestly exceeded it. Studies often did not adjust for differing lengths of follow-up, which seriously skews the data for a procedure where length of follow-up is so important for assessing procedural durability. In addition, many studies are prone to using intermediate outcomes when evaluating venous surgery because of the lengthy follow-up required for documenting final outcomes such as ulcer recurrence. However, it is unclear whether the long-term results for this type of surgery are very different from the results obtained in the short-term.

A number of authors have noted the discrepancy between objective and subjective measures in judging the outcome of venous reconstructive surgery [29, 55, 58]. Often patients heal despite failure of vein grafts and this could be due to changes in activity or increased compliance with compression following surgery, compared to the low rate of compliance seen in conservative treatment alone [55, 84]. A slowly occluding bypass graft may allow sufficient time for recanalisation or for the development of collaterals so that improvement is maintained despite functional obliteration of the graft [54]. Therefore, distinguishing clinical deterioration due to recurrence of valve insufficiency from that which develops in the absence of reflux and is due to other causative factors can be problematic if the function of corrected valves is not reported at follow-up [50].

In addition, patients may be asymptomatic after surgery because they have reduced their physical activity to compensate for the continuing disability rather than because they have improved venous function. Thus, it is also important to document pre- and post-operative activity levels in patients [58]. Post-operative pain and quality of life

measures were rarely mentioned in the included studies so it is unclear what extra discomfort is connected with undergoing surgery in patients who present with only mild symptoms of CVI. It is surprising that so few studies quantify improvements in quality of life when CVI is often associated with severe debilitation, and the recommended basis for undertaking an invasive surgical procedure is the patient's symptomatic rather than clinical need. Since the CEAP classification system incorporates a simple disability score, it should not be difficult to incorporate this information into studies.

While it may be problematic to attribute the reason for surgical success in patients with deep vein incompetence, it is equally difficult to determine the reason for operative failure. For example, transplantation may fail because the transplanted segment itself is either too weak or small in diameter to handle the pressure in the recipient vein; because disruption of the vasa vasorum during vein harvesting rendered the donor segment partially ischaemic; or because the resection and transplantation process made the vein segment more susceptible to early thrombosis [55]. Thus, more detailed study is required to discern what factors, other than graft patency, may be responsible for clinical improvement or deterioration in CVI surgery.

Health policy implications

In Canada there are a relatively small number of CVI patients requiring surgery for deep venous incompetence. This, together with the highly specialised nature of the surgical techniques, has meant that while some surgeons in large urban centres in Canada do perform the occasional deep venous reconstruction, it is more the exception than the rule (personal communication Dr T. Forbes; Dr F. Leoni). Nevertheless, this small group of patients have usually failed all other non-surgical and surgical therapies and still have recalcitrant ulceration that needs treatment. The failure of previous treatments may in part be due to problems patients have with maintaining compression therapy and post-SVS physiotherapy regimens. It is possible that a greater focus on explaining the treatment options available to patients at the outset, and outlining the potential disadvantages of deep venous surgery more clearly (pain, need for general anaesthetic, immobilisation, likelihood of recurrence), may improve compliance with treatments offered earlier in the course of the disease. While it is important to know whether surgery for deep venous incompetence is efficacious and durable, in this context it is equally important to quantify why less invasive treatments have failed in this select patient group.

CONCLUSIONS

A variety of procedures ranging from SVS and SEPS through to deep venous reconstruction (including valvuloplasty, transplantation and transposition) were reported for the treatment of deep venous incompetence. However, deficiencies in reporting, methodological weakness and marked inter-study heterogeneity with respect to patient selection, post-operative management, surgical technique, definition of abnormal venous hemodynamics, symptom grading and diagnostic and venous function testing precluded any definitive synthesis of the data. There was limited evidence (level II and III) indicating that combined SVS/valvuloplasty is a relatively safe procedure that is potentially more effective than SVS in preventing ulcer recurrence in patients with primary deep venous incompetence in both the short- and midterm. Evidence for the efficacy of valvuloplasty, bypass, transplantation, SEPS and iliac stenting in the treatment of deep venous icompetence was inconclusive, and the optimal surgery for patients with deep venous obstruction or secondary valvular incompetence remains unclear.

Even though many of these surgical techniques have been around for more than two decades, the rigour and validity of their evidence base is still relatively immature. This is due to the combined effect of the complexity and long-term nature of CVI, the small proportion of CVI patients with refractory ulcer and the very poor quality of research undertaken in this area to date. The latter is difficult to rectify because of problems unique to CVI that make patient selection and ethical surgical comparison problematic. However, even if RCTs are not practicable, valuable data can still be obtained from carefully designed non-randomised comparative studies. Given that controversy still surrounds many aspects of CVI, it is clear that further good quality research in this area is urgently needed. Well-designed studies with comparable patient groups in each study arm, standardised diagnostic work up of patients and detailed reporting of both hemodynamic results and ulcer recurrence rates would be ideal. However, standardised reporting and collection of data in a registry would also be a move forward. In addition, an evidence based treatment algorithm that would define when to perform SVS in patients with mixed or deep venous incompetence and what type of deep venous surgery is considered appropriate for different indications may be helpful.

APPENDICES

APPENDIX A: CEAP CLASSIFICATION OF CVI

Table A.1: CEAP Classification of CVI (adapted from Antignani [85] and Nicolaides [6])

Clinical findings ("C")			
C0 = no visible venous disease		C4 = skin changes without ulceration	
C1 = telangiectases or reticular veins		C5 = skin changes with healed ulceration	
C2 = varicose veins		C6 = skin changes with active ulceration	
C3 = edema			
Etiology ("E")			
E_C = congenital disease			
E_P = primary disease with undetermined cause			
E_S = secondary venous disease with known cause (post-thrombotic, post-traumatic, etc.)			
Anatomic findings ("A")			
	Superficial veins (A_S)		**Deep veins (A_D)**
1	Telangiectases or reticular veins	6	Inferior vena cava
2	Greater (long) saphenous vein above the knee	7	Common iliac
		8	Internal iliac
3	Greater (long) saphenous vein below the knee	9	External iliac
		10	Pelvic - gonadal, broad ligament, etc.
4	Lesser (short) saphenous	11	Common femoral
5	Non-saphenous system	12	Deep femoral
		13	Superficial femoral
		14	Popliteal
		15	Crural - anterior tibial, posterior tibial, peroneal
		16	Muscular - gastrocnemial, soleal, etc.
			Perforating Veins (A_P)
		17	Thigh
		18	Calf
Pathophysiology ("P")			
P_R = reflux	P_O = obstruction		$P_{R,O}$ = reflux and obstruction
Disability score			
"0" = patient who is asymptomatic with no disability		"2" = patient who can work an 8 hour day only with support	
"1" = patient who is symptomatic but can function without support		"3" = patient who is unable to work even with support	

Appendix B: Review Methodology

The review methodology was developed *a priori*. Consequently, some methods described may not have been carried out in the review if they were not applicable to the available data.

Inclusion criteria

Participants

Data was collected on non-pregnant human patients undergoing treatment for deep or mixed deep/superficial/perforator CVI. Pregnant patients were not included because of the bias that may be introduced by the altered venous physiology associated with pregnancy. Studies that included patients with other indications for surgery, such as arterial disease or superficial CVI with no deep vein involvement, were excluded unless the data subset for the patients with deep or mixed deep/superficial/perforator CVI could be separated from the aggregate data. Animal studies were not included for review.

Index Intervention

Any surgical procedure or combination of surgical procedures used to treat patients with deep or mixed deep/superficial/perforator CVI.

Comparative intervention

Any medical, mechanical or surgical intervention designed to treat patients with deep CVI. Placebo and no treatment comparisons were also included as were studies comparing different operative and post-operative treatment regimens within the same surgical modality.

Outcomes

The papers included must contain information on at least one of the following outcomes of the new or comparative intervention. In addition, at least one of these outcomes must be reported for both the index and the comparative intervention to allow for comparison between the treatment groups. These outcomes may include but not be limited to:

- Perioperative and post-operative mortality of patients (short- and long-term)
- Perioperative and post-operative morbidity of patients which may include, but not be limited to:
  - wound infection;
  - nerve damage;
  - hemorrhage.

- Perioperative and early post-operative efficacy measures which may include, but not be limited to:
  - operative time;
  - discomfort and/or pain;
  - ulcer healing rate;
  - changes in ulcer size or area;
  - ulcer free interval;
  - recurrence or persistence of ulceration;
  - need for further treatment;
  - continued need for external support;
  - changes in any of several clinical grading systems (CEAP score, visual analog scales, quality of life questionnaires);
  - patient satisfaction measured by a defined and validated global assessment scale.
- Evaluation of hemodynamics and morphology which may include, but not be limited to:
  - duplex Doppler ultrasonography;
  - phlebography;
  - foot volumetry;
  - plethysmography.
- Convalescence of patients which may include, but not be limited to:
  - convalescence period;
  - time to independent ambulation;
  - length of hospital stay.

Types of studies

Randomised controlled trials (RCTs) and non-randomised comparative studies were included for review. Only full, peer-reviewed articles were included because abstracts do not provide adequate detail on patient selection, allocation, study design, outcome and measurement methods to allow an accurate, unbiased assessment and comparison of the study results.

Background Information

Where appropriate, relevant published material in the form of narrative reviews, letters, conference material, commentary, editorials and abstracts were included as background information.

Literature search strategy

The medical literature was searched to identify relevant studies and reviews. Searches were conducted without language restriction (Table B.1). Studies were date restricted to 1990 onwards to ensure that the data accurately reflected the level of sophistication currently available in the diagnostic imaging techniques used to select potential surgical candidates. The bibliographies of all publications retrieved in full hard copy form were manually searched for relevant references that may have been missed in the database searches.

Literature database

Study selection was conducted by one reviewer (AS). Articles were excluded that, on the basis of their abstract, clearly did not meet the inclusion criteria. Copies of the full text of potentially eligible studies were retrieved. In some cases, when the full text of the article was retrieved, closer examination revealed that it did not meet the inclusion criteria specified by the review protocol. Consequently these papers were not used to formulate the evidence base for the systematic review (Appendix C). However, relevant information contained in these excluded papers was used to inform and expand the review discussion.

Assessment methods

Study methodology appraisal

The study design of all the included papers was categorised according to the Hierarchy of Evidence [86] in Appendix E. When the study design was mixed (such as when it was unclear whether controls were concurrent or historical) and, therefore, overlapped two categories in the Hierarchy of Evidence, the study was designated as the lower level of evidence. This was considered appropriate because a study is only as methodologically robust as the weakest elements in its study design, and it can be argued that a mixed III-2/III-3 study that has been 'contaminated' with historical controls is no better than a III-3 study, and may even be worse.

Methodological aspects of the included trials were assessed using the quality assessment checklist designed by Downs and Black [87]. This checklist was rigorously developed and demonstrated high internal consistency, good test-retest and inter-rater reliability, and high criterion validity [87]. Following the example of Merlin et al. [88], the checklist was modified by removing the five items relating to the power subscale. Power was calculated independently. The assessment of studies using the unmodified checklist produces a Quality Index score (total = 27). However, given the potential

dangers of using numerical scores to evaluate the quality of trials [89, 90], the scoring system was abandoned in favour of a simple nominal rating scale. When systematic reviews and meta-analyses were available, aspects of their scientific quality were assessed using a validated checklist developed by Oxman and Guyatt [91].

The study quality assessments were undertaken by two independent reviewers (AS and PC) and any disagreements that could not be resolved by discussion were referred to a third reviewer for mediation until consensus was reached. The two reviewers discussed the checklists with respect to the interpretation of questions prior to assessing the studies. Critical appraisal results for all included studies are tabulated in Appendix F.

Outcome measures and data extraction

Study profile information as well as safety and efficacy data were extracted by one reviewer (AS) using standardised data extraction forms developed *a priori*.

In terms of efficacy, the question was whether the index intervention produced equivalent clinical outcomes, in comparison to the comparator procedure. Perioperative efficacy data included the length of hospital and operative time while post-operative efficacy indicators included ulcer free interval and recurrence rate, need for further treatment, and quality of life factors. If any other efficacy outcome was reported in the study it was also tabulated.

The question of safety was addressed in terms of whether the index intervention was more or less likely to cause injury or harm to the patient, in comparison to the comparator procedure. This aspect was considered a subsidiary aim of the review. However, most surgical procedures are invasive and are consequently associated with an increased safety risk that may offset any efficacy benefits. Therefore, it was considered pertinent to tabulate any outcome that affected patient safety.

Data analysis and statistical methods

Data were only reported if they were stated in the text, tables, graphs or figures of the article, or could be accurately extrapolated from the data presented. Conversely, if a particular complication was not reported, it was assumed to be unreported rather than not having occurred. For example, if the mortality rate was not reported in a study, no value was tabulated. This was done to avoid the bias caused by incorrectly assigning a value of zero to an outcome measurement on the basis of an unverified assumption.

The analyses for binary and continuous outcomes included all patients with available data, using the last reported observed response. Thus, the data analysis was by treatment rather than intention-to-treat. The denominator used to calculate proportions was the number of patients remaining in the study at each follow-up period, and did not include dropouts or withdrawals.

It was planned to conduct a meta-analysis on RCT results, when available, if the studies had comparable outcomes, inclusion criteria, treatment regimen and follow-up period. Studies were only included if outcomes were reported across more than two RCTs or where more than two RCTs reported a non-zero value for the outcome. Where possible, a sub-group analysis of the data from both RCTs and non-randomised comparative studies was conducted to ascertain the effects of CVI etiology, symptoms, and anatomic location on patient outcomes. An additional analysis of the results with respect to study design and co-interventions was also conducted, where possible.

Given that there was no pre-defined 'control' for comparison with the surgical interventions for deep or mixed deep/superficial/perforator incompetence in this review, the control intervention for these calculations was taken as the procedure defined as such by the study authors. In studies with multiple comparisons where no such determination was provided, the SVS procedure, valvuloplasty, or the procedure performed on the greatest number of patients was considered to be the control intervention. When overlapping patient groups were reported in studies, only the paper quoting the most complete data set was used.

The heterogeneity between trials would be analysed, where applicable, both qualitatively and by graphical means with χ^2 tests. Since statistical tests of heterogeneity lack power, $p < 0.1$ was used to indicate significant heterogeneity [92, 93]. When there was no significant heterogeneity a fixed effect model was used to calculate the summary relative risks (RR) and absolute risk reduction (ARR) (dichotomous data), weighted or standardised mean difference (continuous data), and 95% confidence intervals (CI), otherwise a random effects model was used [92]. Results were interpreted such that the index intervention was better than the control intervention when the upper limit of the 95% CI was <1 for the RR and <0 for the ARR or weighted or standardised mean difference. All meta-analysis statistics will be calculated with RevMan 4.1 (Update Software Ltd. 1999).

Expert review

External reviewers with clinical expertise in vascular surgery and health technology assessment methodologies evaluated the draft review and provided feedback. In selecting reviewers, the practice of the AHFMR is to choose experts who are well recognised and published in the peer-reviewed literature, and who can offer a provincial and/or national perspective with respect to the use or practice of surgery for CVI.

Table B.1: Databases and search terms used in the search strategy

Database	Platform	Edition	Search Terms[†]
The Cochrane Library		Issue 2, 2003	(venous insufficiency OR postphlebitic syndrome OR venous incompetence OR chronic venous disease) AND (surgery OR transplantation)
CINAHL	Ovid	Week 1/1982 to Week 1, July /2003	#1 exp vein insufficiency/[Surgery, Therapy] #1 exp venous insufficiency/[Surgery, Therapy] #2 exp phlebitis/[Surgery, Therapy] #3 exp varicose veins/[Surgery, Therapy] #4 exp vein/ #5 exp vascular surgery/ #6 (4 OR 5) AND 1 #7 exp saphenous vein/ #8 exp popliteal vein/ #9 exp femoral vein/ #10 (7 OR 8 OR 9) AND (surgery OR therapy OR transplantation).mp [mp = title, CINAHL subject headings, abstract, instrumentation] #11 10 AND 1 #12 (cross-femoral bypass OR cross-femoral venous bypass OR femoro-femoral crossover bypass).mp #13 (femoro-femoral cross-over saphenous bypass OR valvular transposition OR Palma procedure OR Dale Palma OR Dale procedure OR Palma operation).mp #14 (deep vein valvuloplasty OR vein ligation OR stab avulsion OR saphenous vein stripping OR internal valvuloplasty).mp #15 (vein valve transplantation OR vein valve transposition OR iliac vein bypass OR saphenopopliteal bypass).mp #16 (saphenous vein crossover bypass OR saphenous vein cross-over bypass OR subfascial endoscopic perforator).mp #17 (subfascial AND (ligation OR perforat* OR endoscope*)).mp #18 (deep vein valvuloplasty OR stab avulsion OR internal valvuloplasty).mp #19 1 OR 2 OR 3 OR 6 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 (416) #20 clinical trial/ #21 randomized controlled trial/ #22 meta analysis/ #23 exp practice guideline/ #24 exp comparative study/ #25 multicenter study/ #26 exp evaluation/ #27 19 AND (20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26)

Database	Platform	Edition	Search Terms†
EMBASE	Ovid	Week 1/1988 to Week 27/2003	#1 exp vein insufficiency/[Surgery, Therapy] #2 exp phlebitis/[Surgery, Therapy] #3 exp varicosis/[Surgery, Therapy] #4 exp vein/ AND venous insufficiency.mp [mp = title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name, device trade name] #5 exp vascular surgery/ AND venous insufficiency.mp #6 (cross-femoral bypass OR cross-femoral venous bypass OR femoro-femoral crossover bypass).mp #7 (femoro-femoral cross-over saphenous bypass OR valvular transposition OR Palma procedure OR Dale Palma OR Dale procedure OR Palma operation).mp #8 (deep vein valvuloplasty OR vein ligation OR stab avulsion OR saphenous vein stripping OR internal valvuloplasty).mp #9 (vein valve transplantation OR vein valve transposition OR iliac vein bypass OR saphenopopliteal bypass).mp #10 (saphenous vein crossover bypass OR saphenous vein cross-over bypass OR subfascial endoscopic perforator).mp #11 (subfascial AND (ligation OR perforat* OR endoscope*)).mp #12 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 #13 ("clinical trial" OR "randomized controlled trial" OR exp controlled study/ OR "meta-analysis" OR exp practice guideline/ OR exp comparative study/ OR "multicenter study" OR exp evaluation/) #14 #12 AND #13 #15 (exp saphenous vein/ OR exp popliteal vein/ OR exp iliac vein/ OR exp femoral vein/) AND (surgery OR therapy OR transplantation).mp AND venous insufficiency.mp #16 #14 OR #15

Database	Platform	Edition	Search Terms†
PubMed	NLM	Searched 03/07/03	#1 venous insufficiency/surgery[MeSH] OR venous insufficiency/transplantation[MeSH] OR postphlebitic syndrome/surgery[MeSH] OR postphlebitic syndrome/transplantation[MeSH] OR (varicose veins/surgery[MeSH] AND venous insufficiency) OR (varicose veins/transplantation[MeSH] AND venous insufficiency) OR (varicose ulcer/surgery[MeSH] AND venous insufficiency) OR (veins/transplantation[MeSH] AND venous insufficiency) OR (vascular surgical procedures AND venous insufficiency) #2 comparative study OR evaluation studies OR multicenter study OR controlled clinical trial OR (clinical trial OR meta-analysis OR practice guideline OR randomized controlled trial) NOT case report #3 venous insufficiency OR postphlebitic syndrome OR "chronic venous insufficiency" OR "chronic venous disease*" OR "venous incompetence" OR "post-thrombotic syndrome" OR "post-phlebitic syndrome" OR varicose ulcer #4 saphenous vein/surgery[MeSH] OR popliteal vein/surgery[MeSH] OR iliac vein/surgery[MeSH] OR femoral vein/surgery[MeSH] OR saphenous vein/transplantation[MeSH] OR popliteal vein/transplantation[MeSH] OR iliac vein/transplantation[MeSH] OR femoral vein/transplantation[MeSH] OR "cross-femoral bypass" OR "cross-femoral venous bypass" OR "femoro-femoral crossover bypass" OR "femoro-femoral cross-over bypass" OR "femoro-femoral cross-over saphenous bypass" OR "valvular transposition" OR Palma procedure" OR "Dale Palma" OR "Dale procedure" OR "Palma operation" OR "deep vein valvuloplasty" OR "vein ligation" OR "stab avulsion" OR "saphenous vein stripping" OR "internal valvuloplasty" OR "vein valve transplantation" OR "vein valve transposition" OR "iliac vein bypass" OR "saphenopopliteal bypass" OR "saphenous vein crossover bypass" OR "saphenous vein cross-over bypass" OR "subfascial endoscopic perforat*" OR (subfascial AND (ligation OR perforat* OR endoscop*)) #5 #3 AND #4 (In process OR Publisher supplied) records #6 ((#3 AND #4) AND #2)) OR (#1 AND #2) #7 #5 OR #6 #8 (varicose OR leg OR foot OR ischemi* OR ischaemi*) AND (ulcer OR ulcers OR ulceration*) AND (angioplasty OR stent* OR valvuloplasty OR bypass OR by-pass OR graft OR surgery OR surgical OR transposition OR transplantation) #9 (#2 AND #8) OR (related articles for PubMed ID 9615161) OR #7

Database	Platform	Edition	Search Terms[†]
Science Citation Index	Web of Science	01/01/1975 to 09/07/03	(venous insufficiency OR postphlebitic syndrome OR chronic venous disease) AND (surgery OR transplantation OR transposition)
NHS CRD		Searched 09/07/03	venous insufficiency OR postphlebitic syndrome OR chronic venous disease
NLM Gateway		Searched 09/07/03	("venous insufficiency" OR "postphlebitic syndrome") AND (surgery OR transplantation)
TRIP Database		Searched 16/07/03	venous insufficiency
HTA agencies, research registers and guidelines sites		Searched 16/0703	Web sites of HTA agencies, research registers and guidelines sites were also searched.

Note: * is a truncation character that retrieves all possible suffix variations of the root word e.g. surg* retrieves surgery, surgical, surgeon, etc. In databases accessed via the Ovid platform the truncation character is $; [†]Searches limited to human
Abbreviations: HTA - health technology assessment

Appendix C: Excluded Studies

Table C.1: Summary of excluded studies

Study	Study Type	Reason for Exclusion
Abidia & Hardy [13]	Systematic review	The systematic review only included one RCT (Belcaro [94]) that was excluded from the current review because it was superseded by a later publication from the same authors (Belcaro et al. [51]). In addition, the scope of the systematic review was narrower than the current review, both in terms of the interventions studied and the types of studies included.
Adam et al. [95]	Case series	Not a comparative study.
Åkesson et al. [96]	Non-randomised comparative study/case series	Two different surgeries were performed but the results for each patient group could not be separated from the aggregate data.
Åkesson et al. [97]	Case series	Not a comparative study.
Almgren [98]	Review	Review of the results of various case series studies published by the author.
Augustin et al. [99]	RCT	Not a surgical procedure.
Belcaro & Errichi [100]	RCT	Only included patients with superficial venous incompetence.
Belcaro [94]	RCT	Duplication of data presented in later papers (Belcaro et al. [51,101])
Belcaro et al. [101]	RCT	Duplication of data presented in a later paper (Belcaro et al. [51])
Belcaro et al. [102]	Non-randomised comparative study	Over half of the patients had deep venous incompetence but their results could not be separated from the aggregate data.
Belcaro et al. [103]	RCT	Only included patients with superficial venous incompetence.
Bergan et al. [104]	Case series	Not a comparative study.
Brethauer et al. [105]	Non-randomised comparative study	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Burger et al. [106]	RCT	Arterial not venous reconstruction.
Campanello et al. [107]	Randomised case-control study	Only included patients with superficial venous incompetence.

Table C.1: Summary of excluded studies (cont'd)

Study	Study Type	Reason for Exclusion
Chandler et al. [108]	Non-randomised comparative study	Only included patients with superficial venous incompetence.
Chang et al. [109]	RCT	Arterial not venous insufficiency.
Ciostek et al. [110]	Non-randomised comparative study	Only treated patients with superficial venous incompetence.
Dahlstrøm et al. [111]	Case series	Not a comparative study.
Dardik et al. [112]	Non-randomised comparative study	Arterial not venous revascularisation.
Dardik et al. [113]	Non-randomised comparative study	Arterial not venous revascularisation.
DePalma & Kowallek [114]	Non-randomised comparative study	Some patients had deep venous incompetence but their results could not be separated from the aggregate data.
Duhra et al. [115]	RCT	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Dunn et al. [116]	Non-randomised comparative study	The results of patients with superficial and deep venous incompetence and those with arterial ischemia were pooled, and the results for the patients with only deep venous incompetence could not be separated from the aggregate data.
Durkin et al. [117]	RCT	Only treated patients with superficial venous incompetence.
Dwerryhouse et al. [118]	RCT	Only treated patients with superficial venous incompetence.
Einarsson et al. [119]	RCT	Only treated patients with superficial venous incompetence.
Falanga et al. [120]	RCT	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Feinglass et al. [121]	Non-randomised comparative study	Arterial not venous revascularisation.
Fitridge et al. [122]	RCT	Only included patients with superficial venous incompetence.
Fukuoka et al. [123]	Non-randomised comparative study	Over half of the patients had deep venous incompetence but their results could not be separated from the aggregate data.

Table C.1: Summary of excluded studies (cont'd)

Study	Study Type	Reason for Exclusion
Gibbs et al. [124]	RCT	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Gillespie et al. [125]	Non-randomised comparative study/case series	A small subset of patients in both intervention groups had mixed venous insufficiency. While their data could be separated from the aggregate data that included patients with superficial venous insufficiency only, different outcomes were reported for the two intervention groups which precluded any comparison between them.
Guarnera et al. [126]	Case series	Not a comparative study.
Hammersten et al. [127]	RCT	Only treated patients with superficial venous incompetence.
Harrington et al. [128]	Non-randomised comparative study	Arterial not venous revascularisation.
Holme et al. [129]	RCT	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Hoshino et al. [130]	Case series	Not a comparative study.
Iafrati & O'Donnell [39]	Review	Review of case series studies.
Jones et al. [131]	RCT	Only treated patients with superficial venous incompetence.
Jones & Nelson [132]	Systematic review	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Kalra et al. [133]	Case series	Not a comparative study.
Kuan et al. [134]	RCT	Only treated patients with superficial venous incompetence.
Lacroix et al. [135]	Non-randomised comparative study	Some patients had deep venous incompetence but their results could not be separated from the aggregate data.
Lacroix et al. [136]	RCT	Only included patients with superficial venous incompetence.
Lane et al. [73]	Non-randomised comparative study	Some patients had deep venous incompetence but their results could not be separated from the aggregate data.
Lindgren et al. [137]	RCT	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.

Table C.1: Summary of excluded studies (cont'd)

Study	Study Type	Reason for Exclusion
MacKenzie et al. [138]	Non-randomised comparative study	Some patients had deep venous incompetence but their results could not be separated from the aggregate data.
Mahajan & Mosley [139]	Non-randomised comparative study	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Manfrini et al. [140]	Non-randomised comparative study	Only treated patients with superficial venous incompetence.
Mol et al. [141]	Case series	Not a comparative study.
Moor et al. [142]	RCT	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Moreau [143]	Non-randomised comparative study	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Neglen et al. [144]	RCT	Only treated patients with superficial venous incompetence.
Nelzén [145]	Case series	Not a comparative study.
Noel et al. [146]	Case series	Not a comparative study.
Perrin [147]	Non-randomised comparative study	Duplication of data presented in a later paper (Perrin et al. [60])
Perrin [148]	Multiple single arm studies	Abstract only.
Perrin [149]	Non-randomised comparative study	Comparison by indication not by surgery type.
Perrin [67]	Review	Review of case series studies.
Perrin [150]	Non-randomised comparative study	Only treated patients with superficial venous incompetence.
Pierik et al. [151]	RCT	Over half of the patients had deep venous incompetence but their results could not be separated from the aggregate data.
Proebstle et al. [152]	Non-randomised comparative study	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Raju et al. [81]	Non-randomised comparative study	Duplication of data presented in later papers (Raju et al. [47, 153])
Raju et al. [153]	Non-randomised comparative study	The number of patients/limbs that initially underwent each individual surgical procedure was not clearly stated.

Table C.1: Summary of excluded studies (cont'd)

Study	Study Type	Reason for Exclusion
Raju et al. [47]	Non-randomised comparative study	Extension of data presented in an earlier paper (Raju et al. [153]). However, results for the individual surgical procedures could not be separated from the aggregate data.
Raju et al. [154]	Case series	Not a comparative study.
Raju et al. [155]	Non-randomised comparative study	Over half of the patients had deep venous obstruction but their results could not be separated from the aggregate data.
Rehman et al. [156]	RCT	Only treated patients with uncomplicated long saphenous varicose veins.
Rivlin et al. [157]	Non-randomised comparative study	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Robinson et al. [158]	Non-randomised comparative study	Only treated patients with superficial venous incompetence.
Ruffieux et al. [159]	Non-randomised comparative study	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Rutgers & Kitslaar [160]	RCT	Only treated patients with superficial venous incompetence.
Sabolinski et al. [161]	Non-randomised comparative study	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Samson et al. [162]	Non-randomised comparative study	Only treated patients with superficial venous incompetence.
Sarin et al. [163]	RCT	Only treated patients with superficial venous incompetence.
Sarin et al. [84]	RCT	Only treated patients with superficial venous incompetence.
Sato et al. [164]	Non-randomised comparative study	Over half of the patients had deep venous incompetence but their results could not be separated from the aggregate data.
Schanzer & Skladany [165]	Non-randomised comparative study	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Sottiurai [166]	Non-randomised comparative study	Duplication of data presented in a later paper (Sottiurai [61])
Sparks et al. [167]	Case series	Not a comparative study.

Table C.1: Summary of excluded studies (cont'd)

Study	Study Type	Reason for Exclusion
Stuart et al. [168]	Non-randomised comparative study	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Stuart et al. [169]	Non-randomised comparative study	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Sybrandy et al. [170]	RCT	Over half of the patients had deep venous incompetence but their results could not be separated from the aggregate data.
Sykes et al. [171]	RCT	Only included patients with superficial venous incompetence.
Teepe et al. [172]	RCT	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Travers et al. [173]	Non-randomised comparative study	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
Travers & Makin [174]	RCT	Specific patient indications not stated so unable to determine whether patients had superficial, deep or mixed venous insufficiency.
van Dijk et al. [175]	RCT	Arterial not venous reconstruction.
Warburg et al. [176]	RCT	Over half of the patients had deep venous incompetence but their results could not be separated from the aggregate data.
Zamboni et al. [177]	Non-randomised comparative study	Only included patients with superficial venous incompetence.

Table C.2: Summary of potentially relevant foreign language studies that were not translated

Study	Language	Study Type	Comments
Dmitriev et al. [178]	Russian	Possible non-randomised comparative study	Report on 30 surgical interventions for chronic venous insufficiency.
Ge et al. [179]	Chinese	Non-randomised comparative study	Evaluation of three kinds of valvuloplasty in 62 patients with venous reflux disease.
Gladkikh et al. [180]	Russian	Non-randomised comparative study	Report on four methods for valve correction in 241 patients with valvular incompetence of the deep veins as follows: correction with a lavsan spiral (70 operations), suturing with paravasal structures (59 operations), three-ligature method (142 operations) and an original method with shortening of the cusps without venotomy (30 operations).
Gruss [181]	German	Non-randomised comparative study	Results for 36 reconstructive valve repair procedures (direct valvuloplasty, transposition and transplantation) are reported.
Nachbur et al. [182]	German	Possible non-randomised comparative study	No abstract available.

APPENDIX D: EXPLANATION OF STATISTICS (adapted from Jaenschke et al. [183])

The RR is the risk of an outcome (for example, ulcer) occurring after the intervention (in this case surgery) as a percentage of the original risk.

Table D.1: Sample 2x2 table

	Outcome		Total Number of Patients
Study	Yes	No	
Intervention	A	B	A+B
Control	C	D	C+D

From Table D.1, RR is calculated as follows:

$$RR = [A/(A+B)]/[C/(C+D)]$$

The difference in the risk of the outcome between the two patient groups is the absolute risk reduction and is the proportion of patients who do not experience the outcome in question as a result of being treated with the index intervention rather than the control. From Table D.1, ARR is calculated as follows:

$$ARR = [A/(A+B)] - [C/(C+D)]$$

Worked example

The ulcer recurrence rates for patients undergoing SVS plus valvuloplasty versus SVS reported by Sottiurai et al. [61], after a mean follow-up period of 37 months, are listed in Table D.2.

Table D.2: Ulcer recurrence rates reported by Sottiurai et al. [61]

	Recurrent Ulcer		Total Number of Patients
Intervention	Yes	No	
SVS plus valvuloplasty	4	17	21
SVS	19	14	33

For this example,

$$RR = [4/(17+4)]/[19/(19+14)]$$
$$= 0.33$$
$$ARR = [4/(17+4)] - [19/(19+14)]$$
$$= -0.39$$

This means that the RR of having a recurrent ulcer after SVS plus valvuloplasty is 33%, that is, about a third of the risk of those undergoing SVS. The ARR is 39%, which is the number of patients in the SVS plus valvuloplasty group who will be spared having a recurrent ulcer, compared to those in the SVS group.

The RR had an associated 95% CI of 0.13 to 0.84 while the ARR 95% CI ranged from -0.62 to -0.15 (calculations not shown here). When the upper limit of the 95% CI is <1 for the RR and <0 for the ARR it means that the index intervention is better than the control intervention, and that this result is statistically significant ($p < 0.05$). The converse is true when the lower limit of the 95% CI for the RR or ARR is >1 or >0, respectively. When the 95% CI spans one for RR (e.g. 95% CI 0.45 to 1.57) or zero for ARR (e.g. 95% CI -0.42 to 0.23) there is no statistically significant difference between the two treatment groups for that outcome.

APPENDIX E: HIERARCHY OF EVIDENCE

Table E.1: Designation of levels of evidence [86]

Level of Evidence	Study Design
I	Evidence obtained from a systematic review of all relevant randomised controlled trials.
II	Evidence obtained from at least one properly designed randomised controlled trial.
III-1	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time-series with a control group.
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group.
IV	Evidence obtained from case-series, either post-test or pre-test/post-test.

APPENDIX F: STUDY QUALITY ASSESSMENT RESULTS

STUDY QUALITY ASSESSMENT CHECKLIST (adapted from Downs and Black [87])

Reporting

1. *Is the hypothesis/aim/objective of the study clearly described?*
2. *Are the main outcomes to be measured clearly described?*

   If the main outcomes are first described in the Results section, the question should be answered no.
3. *Are the characteristics of the patients included in the study clearly described?*

   In RCTs and non-randomised comparative studies inclusion and/or exclusion criteria should be given. In case-control studies, a case-definition and the source for controls should be given.
4. *Are the interventions of interest clearly described?*

   Treatments and placebo (where relevant) that are to be compared should be clearly described. If any of the treatments are described by name only with no further detail given, the question should be answered no.
5. *Are the distributions of principal confounders in each group of subjects to be compared clearly described?*

   The question should be answered yes if a list of principal confounders is provided; a statistical comparison of preoperative parameters for the patient groups was reported; or a minimum of set of preoperative patient parameters is reported for all patient groups which must include age distribution, gender mix, and at least one of the following: hemodynamic parameter, patient co-morbidities, distribution of incompetence, type of incompetence, history of ulceration, or history of previous venous surgery.
6. *Are the main findings of the study clearly described?*

   Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions (this question does not cover statistical tests which are considered below).
7. *Does the study provide estimates of the random variability in the data for the main outcome(s)?*

   In non-normally distributed data the inter-quartile range of results should be reported. In normally distributed data the standard error, standard deviation, or confidence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimates used were appropriate and the question should be answered yes.

8. *Have all important adverse events that may be a consequence of the intervention been reported?*

   This should be answered yes if the study mentions the presence or absence of adverse events in the patient groups during the follow-up period.

9. *Have the characteristics of patients lost to follow-up been described?*

   This should be answered yes where there were no losses to follow-up or where losses to follow-up were so small (< 10% in each treatment group) that findings would be unaffected by their inclusion. This would be answered no where a study does not report the number of patients lost to follow-up.

10. *Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is <0.001?*

External validity

11. *Were the subjects asked to participate in the study representative of the entire population from which they were recruited?*

    The study must identify the source population for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients or a random sample. Random sampling is only feasible where a list of all members of the relevant population exists. Where a study does not report the proportion of the source population from which the patients are derived, the question should be answered as 'unable to determine'. If there is no information provided on the source population at all, the question should be answered no.

12. *Were those subjects who were prepared to participate in the study representative of the entire population from which they were recruited?*

    The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the main confounding factors was the same in the study sample and the source population. In cases where there is insufficient information to decide, the question should be answered as 'unable to determine'.

13. *Were the staff, places, and facilities where the patients were treated representative of the treatment the majority of patients receive?*

    For the question to be answered yes the study should demonstrate that the intervention was representative of that in use in the source population. The question should be answered no if, for example, the intervention was undertaken in a specialist centre unrepresentative of the hospitals most of the source population would attend. In cases where there is insufficient information to decide, the question should be answered as 'unable to determine'.

Internal validity - bias

14. *Was an attempt made to blind study subjects to the intervention they received?*

    For the studies where the patients would have no way of knowing which intervention they received, this should be answered yes. For studies that do not state whether blinding was attempted the answer should be 'unable to determine'.

15. *Was an attempt made to blind those measuring the main outcomes of the intervention?*

16. *If any of the results of the study were based on "data dredging" was this made clear?*

    Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned sub-group analyses were reported then answer yes.

17. *Do the analyses adjust for different lengths of follow-up of patients?*

    Where follow-up was the same for all study patients the answer should be yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where difference in follow-up are ignored should be answered no.

18. *Were the statistical tests used to assess the main outcomes appropriate?*

    That statistical techniques used must be appropriate to the data. For example, non-parametric methods should be used for small sample size. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.

19. *Were the main outcome measures used valid and reliable?*

    For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrate the outcome measures are accurate, the question should be answered yes.

Internal validity - confounding

20. *Were the patients in different study arms recruited from the same patient population?*

    For example, patients for all comparison groups should be selected from the same hospital. The question should be answered 'unable to determine' for case-control and non-randomised comparative studies where there is no information concerning the source of patients included in the study.

21. *Were the patients in different study arms recruited over the same period of time?*

    For a study that does not specify the time period over which patients were recruited, the question should be answered as 'unable to determine'. For a non-randomised comparative trial that has a long study period (at least five years) and does not specify that patients were recruited consecutively, the question should be answered no unless it is clearly stated that all patients who were eligible for inclusion in the study over the study period were recruited.

22. *Were the patients randomised to intervention groups?*

    Studies stating that patients were randomised should be answered yes except where the method of randomisation would not ensure random allocation.

23. *Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?*

    All non-randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.

24. *Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?*

    The question should be answered no for RCTs if:

    - The main conclusions of the study were based on analyses of treatment rather intention-to-treat
    - The distribution of known confounders in the different treatment groups was not described
    - The distribution of known confounders differed between the treatment groups but was not taken into account in the analyses.

    In non-randomised studies, if the effect of the main confounders was not investigated or confounding was demonstrated but not adjusted for in the final analyses the question should be answered no. The question should be answered yes if a study conducts sub-group analyses with respect to at least one of the various confounding factors or addresses the implications of at least one of the confounding factors in the Discussion section.

25. *Were losses of patients to follow-up taken into account?*

    If the numbers of patients lost to follow-up are not reported, the question should be answered as 'unable to determine'. If the proportion lost to follow-up was too small (< 10% in each treatment group) to affect the main findings, the question should be answered yes.

Power

26. *Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is <5%?*

Calculations were based on an ulcer recurrence rate of 30% [39] for patients undergoing surgery for deep venous insufficiency and the assumption that reducing this rate to 15% would be clinically significant.

The minimum number of patients required in each study arm to detect a halving of the ulcer recurrence rate was calculated using the following formula [184]:

$$n = \frac{(p_1q_1 + p_2q_2) \times 7.9}{(p_1 - p_2)^2}$$

where p_1 = frequency of outcome in group 1; $q_1 = 1 - p_1$
p_2 = frequency of outcome in group 2; $q_2 = 1 - p_2$

Setting a significance level of $\alpha = 0.05$ (two-sided) a power of 80% ($\beta = 0.20$) means that at least 118 patients in each study arm would be required to detect a halving of the ulcer recurrence rate.

STUDY QUALITY ASSESSMENT RESULTS

Study Characteristic		Belcaro et al. [51]	Makarova et al. [50]	AbuRahma et al. [54]	Cheatle & Perrin [55]	Danza et al. [56]	Jamieson & Chinnick [29]	Iafrati et al. [57]
Reporting	Is the hypothesis/aim/objective of the study clearly described?	✓	✓	✓	✓	X	✓	✓
	Are the main outcomes to be measured clearly described?	✓	✓	✓	X	X	✓	✓
	Are the characteristics of the patients included in the study clearly described?	✓	✓	✓	✓	✓	X	X
	Are the interventions of interest clearly described?	✓	✓	✓	✓	✓	✓	✓
	Are the distributions of principal confounders in each group of subjects to be compared clearly described?	✓	X	✓	✓	X	X	X
	Are the main findings of the study clearly described?	✓	✓	✓	✓	✓	✓	✓
	Does the study provide estimates of the random variability in the data for the main outcome(s)?	?	NA	✓	X	X	X	X
	Have all important adverse events that may be a consequence of the intervention been reported?	✓	X	✓	✓	✓	✓	✓
	Have the characteristics of patients lost to follow-up been described?	✓	✓	✓	X	✓	✓	✓
	Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is <0.001?	X	X	✓	X	NA	X	X
External validity	Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	X	?	?	?	?	?	?
	Were those subjects who were prepared to participate in the study representative of the entire population from which they were recruited?	?	?	?	?	?	?	?
	Were the staff, places, and facilities where the patients were treated representative of the treatment the majority of patients receive?	?	?	?	?	?	?	?

Study Characteristic		Belcaro et al. [51]	Makarova et al. [50]	AbuRahma et al. [54]	Cheatle & Perrin [55]	Danza et al. [56]	Jamieson & Chinnick [29]	Iafrati et al. [57]
Internal validity *Bias*	Was an attempt made to blind study subjects to the intervention they received?	?	?	?	?	?	?	?
	Was an attempt made to blind those measuring the main outcomes of the intervention?	?	?	?	?	?	?	?
	If any of the results of the study were based on "data dredging" was this made clear?	✓	✓	✓	✓	✓	✓	✓
	Do the analyses adjust for different lengths of follow-up of patients?	✓	✓	✓	X	?	?	X
	Were the statistical tests used to assess the main outcomes appropriate?	?	?	✓	NA	NA	NA	NA
	Were the main outcome measures used valid and reliable?	✓	✓	✓	✓	✓	✓	✓
Confounding	Were the patients in different study arms recruited from the same patient population?	?	?	?	✓	✓	✓	?
	Were the patients in different study arms recruited over the same period of time?	?	✓	?	X	X	✓	✓
	Were the patients randomised to intervention groups?	✓	✓	X	X	X	X	X
	Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?	?	?	X	X	X	X	X
	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	X	X	✓	X	X	X	X
	Were losses of patients to follow-up taken into account?	X	✓	✓	X	✓	✓	✓
Power	Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is <5%?	X	X	X	X	X	X	X

Key: Yes = ✓; No = X; Unable to determine = ?; Not applicable or not possible because of the nature of the intervention = NA

Study Characteristic		Masuda & Kistner [58]	Owens et al. [59]	Perrin [60]	Raju et al. [52]	Sakuda et al. [53]	Sottiurai [61]	Welch et al. [62]
Reporting	Is the hypothesis/aim/objective of the study clearly described?	✓	✓	✓	✓	✓	X	X
	Are the main outcomes to be measured clearly described?	✓	✓	✓	✓	✓	X	✓
	Are the characteristics of the patients included in the study clearly described?	X	✓	X	X	✓	✓	X
	Are the interventions of interest clearly described?	✓	✓	✓	✓	✓	✓	✓
	Are the distributions of principal confounders in each group of subjects to be compared clearly described?	X	X	X	X	✓	X	X
	Are the main findings of the study clearly described?	✓	✓	✓	✓	✓	✓	✓
	Does the study provide estimates of the random variability in the data for the main outcome(s)?	✓	✓	X	NA	✓	X	?
	Have all important adverse events that may be a consequence of the intervention been reported?	✓	X	✓	✓	✓	X	✓
	Have the characteristics of patients lost to follow-up been described?	✓	?	X	?	✓	✓	✓
	Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is <0.001?	✓	✓	✓	X	X	X	X
External validity	Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	?	?	?	?	?	?	?
	Were those subjects who were prepared to participate in the study representative of the entire population from which they were recruited?	?	?	?	?	?	?	?
	Were the staff, places, and facilities where the patients were treated representative of the treatment the majority of patients receive?	?	?	?	?	?	?	?

Study Characteristic		Masuda & Kistner [58]	Owens et al. [59]	Perrin [60]	Raju et al. [52]	Sakuda et al. [53]	Sottiurai [61]	Welch et al. [62]
Internal validity *Bias*	Was an attempt made to blind study subjects to the intervention they received?	?	?	?	?	?	?	?
	Was an attempt made to blind those measuring the main outcomes of the intervention?	?	?	?	?	?	?	?
	If any of the results of the study were based on "data dredging" was this made clear?	X	X	✓	✓	✓	?	✓
	Do the analyses adjust for different lengths of follow-up of patients?	✓	X	X	✓	X	X	X
	Were the statistical tests used to assess the main outcomes appropriate?	✓	✓	✓	✓	✓	?	?
	Were the main outcome measures used valid and reliable?	✓	✓	✓	✓	✓	✓	✓
Confounding	Were the patients in different study arms recruited from the same patient population?	✓	✓	?	✓	?	?	?
	Were the patients in different study arms recruited over the same period of time?	?	X	X	✓	✓	?	?
	Were the patients randomised to intervention groups?	X	X	X	X	X	X	X
	Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?	X	X	X	X	X	X	X
	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	✓	✓	✓	✓	X	X	X
	Were losses of patients to follow-up taken into account?	✓	?	X	?	✓	✓	✓
Power	Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is <5%?	X	X	X	X	X	X	X

Key: Yes = ✓; No = X; Unable to determine = ?; Not applicable or not possible because of the nature of the intervention = NA

APPENDIX G: DATA EXTRACTION TABLES

List of abbreviations for Appendix G

Measurement Abbreviations

SD – standard deviation

Abbreviations for Venous Anatomy

GSV – greater saphenous vein (also called internal or long saphenous vein)

SFV - superficial femoral vein

SSV – small saphenous vein (also called external or short saphenous vein)

General Abbreviations

AVP - ambulatory venous pressure

CEAP - Clinical signs, Etiology, Anatomic distribution, and Pathophysiology

CVI - chronic venous insufficiency

DVT – deep vein thrombosis

FU – follow-up

LAP – limited anterior plication

LDS – lipodermatosclerosis

QOL - quality of life

SEPS - subfascial endoscopic perforator surgery

SVS – superficial venous surgery

Intervention study profile – RCTs

Authors/ Location	Intervention	Study Design	Study Population
Belcaro et al.[51] Irvine Laboratory, St Mary's Hospital at Imperial College, London, UK Cardiovascular Institute, Chieti University, and Angiology and Vascular Surgery and Clinical Trials Unit, Pierangeli Clinic, Pescara, Italy	**1) SVS** Ligation of incompetent superficial veins (including the GSV at its femoral junction) and removal of incompetent venous segments. No further details were stated. **2) SVS (as for group 1 above) plus SFV valvuloplasty** Surgical Access: Transverse inguinal incision exposing the GSV and the common and SFV distal to the femoral vein bifurcation. Anaesthesia: Not stated Surgical Technique: LAP was performed on the anterior side of the common femoral vein after limited dissection of less than 50% of the vein circumference at the level of the sapheno-femoral junction with a no-touch dissection technique. The anterior surface of the common femoral vein was then plicated (3 mm wide stitches) longitudinally over the insertion line of the valve cusp for a length of 5 mm with a single CV-7 Gore-Tex monofilament suture. Intra-operative Assessment of Venous/Valvular Competence: Modified Raju test which involved compressing and milking the common femoral vein 2-3 cm above and below the suture. Fast filling of the vein distal to the valve when proximal compression was released indicated incompetence. Vein Clamping: No clamps were used and the vein was not occluded during the procedure. Anti-thrombotic Protocol: Not used.	Prospective non-blinded randomised concurrently controlled trial Level of Evidence: II Intention-to-Treat Analysis: No - nine patients were lost to follow-up and their data were not included in the final analysis. Method of Randomisation: Not stated Time of Randomisation: After giving informed consent Method of Allocation Concealment: Unclear whether an attempt was made to conceal allocation. Details of Blinding: Not stated Participation Rate: Six (12%) of the initial 50 patients declined to participate because they could not meet the 10 year follow-up requirement. Eligibility Rate for Study: Not stated Follow-up: Annually up to 10 years Lost to Follow-up: **1)** 18.2%; **2)** 22.7% Withdrawals were not due to medical problems; patients were lost or refused to be re-evaluated (specific reasons were not given).	Sample Size: **1)** n = 18; **2)** n = 17 No statistically significant difference between groups 1 and 2 in age, sex distribution, AVP, refill time ($p < 0.05$) or SFV diameter (p not stated). Patient Diagnosis: Primary SFV valve incompetence and signs of venous hypertension (large varicose veins, lipodermatosclerosis, peri-malleolar skin changes). General Diagnostic Definitions: Deep venous incompetence was defined as an increased AVP only partially modified by excluding the superficial system with an ankle tourniquet; significant reflux on standing in the common and SFV lasting longer than three seconds; and the presence of mobile vein cusps or valvular structures 3 cm above or below the femoral vein bifurcation. A normal AVP was defined as < 30 mmHg and a normal refill time was > 18 seconds. Preoperative Mean AVP: *Without cuff:* **1)** 65 mmHg (± 5.0)*; **2)** 65 mmHg (± 6.0)* *With cuff:* **1)** 62 mmHg (± 5.0)*; **2)** 61 mmHg (± 6.0)*

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	Post-operative Management: Subcutaneous calcium heparin and elastic compression stockings were used for five days post-operatively. **1) & 2)** Operation Type: Not stated Adjunctive Surgery: No Preoperative Evaluation: Colour duplex scanning, high resolution ultrasound scanning Post-operative Evaluation: Colour duplex scanning, high resolution ultrasound scanning	Study Period: Not stated Operator Details: Not stated Inclusion Criteria: Primary femoral vein valve incompetence Exclusion Criteria: History of venous thrombosis; obese patients; patients with any vascular, metabolic or cardiac disease	Preoperative Mean Refill Time: *Without cuff:* **1)** 10 seconds (± 3.0)*; **2)** 9 seconds (± 6.0)* *With cuff:* **1)** 11 seconds (± 5.0)*; **2)** 11 seconds (± 4.0)* Preoperative Mean Maximum Venous Outflow: Not stated Type of Incompetence: **1) & 2)** Deep and superficial - 100% Distribution of Incompetence: Not stated Mean Age: **1)** 41 yrs (range 25 to 66) **2)** 41 yrs (range 26 to 61) Gender Mix: **1)** M/F = 11 (61.1%)/ 7 (38.9%) **2)** M/F = 11 (64.7%)/ 6 (35.3%) Clinical Grading: Not stated Patient Co-morbidities: Not stated Patient Details: Not stated Previous Treatment: Not stated

*Paper did not define the variance measure used

Authors/ Location	Intervention	Study Design	Study Population
Makarova et al. [50] Department of Surgery, Urals Medical Academy, and the Sverdlovsk Vascular Centre, Ekaterinburg, Russia	**1) SVS** GSV stripping with stab avulsion of varicose tributaries. Adjunctive Surgery: The SSV was stripped in 1.6% of patients and subfascial perforators were ligated in 33.9%. No further details were stated. **2) SVS (as for group 1 above) plus SFV valvuloplasty** The proximal incompetent SFV valve was corrected with Kistner's technique. Adjunctive Surgery: The SSV was stripped in 3.2% of patients and subfascial perforators were ligated in 31.8%. No further details were stated. **1) & 2)** Operation Type: Unilateral - 100% Preoperative Evaluation: Patients were observed for five years preoperatively with annual clinical and duplex ultrasound scan examinations; the reflux volume index was used for evaluation of reflux severity and dynamics and findings were confirmed by retrograde phlebography in 86 (51.2%) of the 168 patients originally selected for the study. Post-operative Evaluation: Clinical and duplex ultrasound scan examinations	Prospective non-blinded randomised concurrently controlled trial Level of Evidence: II Intention-to-Treat Analysis: No - three patients were lost to follow-up and their data were not included in the final analysis. Method of Randomisation: Not stated Time of Randomisation: After stratification according to the type of clinical dynamics (based on five years of preoperative observation). Method of Allocation Concealment: Unclear whether an attempt was made to conceal allocation. Details of Blinding: Not stated Participation Rate: 128 (76.2%) of 168 patients originally selected for the study. The remainder refused to undergo surgery. Eligibility Rate for Study: 168 of 1,879 patients (8.9%)	Sample Size: **1)** n = 62; **2)** n = 63 Statistical comparison of preoperative parameters for groups 1 and 2 was not reported. However, patients were stratified according to their clinical dynamics prior to randomisation. Patient Diagnosis: Primary CVI with no evidence of post-thrombotic disease. Clinical dynamics were as follows*: **1)** Stable - 33.9%; Progressive - 66.1% **2)** Stable - 34.9%; Progressive - 65.1% General Diagnostic Definitions: Reflux duration > 0.5 seconds was considered pathologic. Preoperative Mean AVP: Not stated Preoperative Mean Refill Time: Not stated Preoperative Mean Maximum Venous Outflow: Not stated Type of Incompetence: **1) & 2)** Superficial - 100%; Deep - 100%; Perforator - 32.8% Distribution of Incompetence : **1) & 2)** (n = 169 extremities) GSV - 100%; SFV - 100%; Popliteal vein - 7.1% Mean Age: Not stated Gender Mix: Not stated

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Authors/ Location	Intervention	Study Design	Study Population
		Follow-up: Range 7 to 8 years Lost to Follow-up: **1)** 3.1%; 2) 1.6% No further details were stated. Study Period: Study participants selected from the pool of patients diagnosed with primary CVI during the period from 1983 to 1984. Operator Details: Not stated Inclusion Criteria: Clinical class C2, C3 or C4 (CEAP classification) and reflux demonstrated by duplex ultrasound scan in both the proximal GSV and the SFV. Exclusion Criteria: Post-thrombotic disease: specifically, a history of DVT, episodes of acute edema of the lower extremity, trauma, major surgery or a hospital stay with bed rest longer than three days. Ultrasound findings of segmental thickening of the venous wall or partial or complete occlusion of veins.	Clinical Grading (CEAP) (n = 128): **1) & 2)** C2 - 39.2%;C3 - 35.2%;C4 - 25.6% Patient Co-morbidities: Not stated Patient Details: Not stated Previous Treatment: Elastic compression was recommended for each patient at the first visit. No details were given with respect to compliance.

*Progressive = if the extremity demonstrated an increase of at least one clinical class by the end of the fifth year in comparison with the initial class of the limb; Stable = no change in clinical class.

Intervention study profile - Non-randomised comparative studies

Authors/ Location	Intervention	Study Design	Study Population
Jamieson & Chinnick [29] Department of Surgery, University of Western Ontario and the Division of Vascular Surgery, London Health Sciences Centre, London, Ontario, Canada	**1) Valvuloplasty** Surgical Access: Not stated Anaesthesia: Not stated Surgical Technique: The common femoral, superficial and deep femoral veins were exposed and mobilised. Valves were identified and repaired with 7-0 Prolene sutures, approximating the sides of the valve insertion. Five to seven interrupted sutures were used on each side. The valve was then encircled with polytetrafluoroethylene, which was loosely secured with interrupted sutures. Intra-operative Assessment of Venous/Valvular Competence: The strip test was performed with the patient in anti-Trendelenburg position. Vein Clamping: Not stated Adjunctive Surgery: Not stated **2) Venous valve transplantation** Surgical Access: Not stated Anaesthesia: Not stated Surgical Technique: A 3 to 4 cm segment of above knee popliteal vein was removed and replaced with a 6 to 7 cm long segment of axillary vein that was sewn in place with eight interrupted Prolene sutures at each anastomosis. The vein was then loosely wrapped with polytetrafluoroethylene. Intra-operative Assessment of Venous/Valvular Competence: Not stated Vein Clamping: Not stated Adjunctive Surgery: Not stated	Retrospective non-randomised comparative study with concurrent controls Level of Evidence: III-2 Intention-to-Treat Analysis: Not stated but intention-to-treat analysis conducted by default since there were no losses to follow-up. Participation Rate: Not stated Eligibility Rate for Study: Not stated Follow-up: Minimum follow-up was two years Lost to Follow-up: 0% Study Period: 1991 to 1992 Operator Details: All operations were performed by a single surgeon. Inclusion Criteria: Not stated Exclusion Criteria: Not stated	Sample Size: (n = 15 patients) **1)** n = 12 limbs; **2)** n = 4 limbs Some preoperative measurements were only available for the combined patient pool of n = 15 (n = 16 limbs). Statistical comparison of preoperative parameters for groups 1 and 2 was not reported. Patient Diagnosis: Patients requiring deep venous valvular repair because of CVI that was refractory to conservative care and removal of incompetent superficial and perforating veins. General Diagnostic Definitions: Not stated Preoperative Mean AVP: Not stated Preoperative Mean Refill Time: Not stated Preoperative Mean Maximum Venous Outflow: Not stated Type of Incompetence: **1)** Primary deep vein valvular insufficiency - 100% **2)** Re-canalised post-phlebitic deep vein valve insufficiency - 100% Distribution of Incompetence: **1)** SFV - 100%; Deep femoral vein - 8.3% **2)** Femoral vein - 100% Mean Age: Not stated Gender Mix: (n = 15 patients) **1) & 2)** M/F = 3 (20.0%)/ 12 (80.0%)

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Authors/ Location	Intervention	Study Design	Study Population
	1) & 2) Anti-thrombotic Protocol: Heparin Operation Type: Bilateral - 6.7% (n = 15 patients) Post-operative Management: Heparin was continued for five days post-operatively. Warfarin was started on post-operative day one and continued for three months. A sequential venous pump was applied in the recovery room, and this was continued until the patient was completely ambulatory (usually 2 to 4 days). Patients were discharged with compression hosiery that provided support of 20 to 30 mmHg. Preoperative Evaluation: Physical examination, ascending and descending phlebography, duplex scanning and air plethysmography Post-operative Evaluation: Clinical examination, duplex scanning and air plethysmography; descending phlebography was performed in four patients (26.7%)		Clinical Grading (n = 16 limbs): *Porter Classification:* **1) & 2)** IV - 31.3%; V - 18.7%; VI - 50.0% *Kistner Classification:* **1) & 2)** III - 19.0%; IV - 81.0% Patient Co-morbidities: Not stated Patient Details: All patients had either reflux to the calf (19.0%) or reflux to the ankle (81.0%). Previous Treatment: **1) & 2)** Conservative care and removal of incompetent superficial and perforating veins - 100%

Authors/ Location	Intervention	Study Design	Study Population
Raju et al. [52] University of Mississippi Medical Center, Jackson, Mississippi, USA	**1) Iliac venous stenting** Surgical Access: Cannulation of the femoral vein was achieved via an ipsilateral femoral venous puncture at the mid-thigh level under ultrasound scan guidance. Anaesthesia: General or local infiltration analgesia in combination with monitored sedation. Surgical Technique: Intravascular ultrasound scanning was used for the identification or confirmation of treatable lesions before stent placement. After balloon dilation of the obstructed region, a 14 or 16 mm stent that corresponded to the size of the healthy disease free iliac vein was deployed to cover the dilated area. Vein Clamping: Not stated Adjunctive Surgery: No **2) Iliac venous stenting (as for group 1 above) plus SVS** Surgical Access: Not stated Anaesthesia: Not stated Surgical Technique: Stripping of the GSV in the thigh (81.8% of limbs - 48.2% of these also had stab avulsion of associated non-truncal varices) or heat closure of the GSV with a radiofrequency probe (8.2% of limbs). Vein Clamping: Not stated Adjunctive Surgery: No	Prospective non-randomised concurrently controlled trial Level of Evidence: III-2 Intention-to-Treat Analysis: No - 13% of limbs were lost to follow-up and their data were not included in the final analysis. In addition, four technical failures that occurred during the study period were excluded from analysis with no reason given. Participation Rate: Not stated Eligibility Rate for Study: Not stated Mean Follow-up: 9 months (range 1 to 41) Lost to Follow-up: **1) & 2)** 13% Study Period: 12/97 to 11/00 Operator Details: Not stated Inclusion Criteria: Not stated Exclusion Criteria: Not stated	Sample Size: (n = 292 patients) **1)** n = 243 limbs ; **2)** n = 61 limbs Some preoperative measurements were only available for the combined patient pool of n = 292 (n = 304 limbs). Statistical comparison of preoperative parameters for groups 1 and 2 was not reported. Patient Diagnosis: Iliac venous stenosis in CVI General Diagnostic Definitions: Not stated Preoperative Mean AVP: Not stated Preoperative Mean Refill Time: Not stated Preoperative Mean Maximum Venous Outflow: Not stated Type of Incompetence: **1) & 2)** (n = 304 limbs) Post-thrombotic lesion - 53.3%; Non-thrombotic lesion - 46.7% **1) & 2)** (n = 304 limbs) Isolated deep venous obstruction - 43.4%; Obstruction with deep venous reflux - 4.9%; Obstruction with deep/perforator reflux - 0.6%; Obstruction with superficial reflux - 21.4%; Obstruction with mixed superficial/perforator/deep reflux - 29.6% Distribution of Incompetence: Not stated Median Age: **1) & 2)** 52 yrs (range 14 to 83) Gender Mix: **1) & 2)** M:F = 1:2

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Authors/ Location	Intervention	Study Design	Study Population
	1) & 2) Intra-operative Assessment of Venous/Valvular Competence: Descending phlebography, pressure measurements, and an intravascular ultrasound investigation were performed to assess the final result. Anti-thrombotic Protocol: Patients received 2,500 U of dalteperin sodium preoperatively and 3,000 to 5,000 U of heparin intravenously during the procedure. Operation Type: Bilateral - 4.1% Post-operative Management: Daily aspirin therapy (81 mg) post-operatively. Warfarin therapy was instituted if a clearly hyper-coagulable state was present, and was continued if the patient was on warfarin therapy prior to surgery. In such cases, warfarin therapy was supplemented with a twice a week dose of 81 mg of aspirin. Preoperative Evaluation: Duplex scan, air plethysmography, ascending or descending trans-femoral phlebography Post-operative Evaluation: Duplex scan, air plethysmography, ascending or descending trans-femoral phlebography, clinical examination		Clinical Grading (CEAP Classification): **1) & 2)** C2 - 7.9%; C3 - 52.0%; C4 - 19.7%; C5 - 4.3%; C6 - 16.1% Patient Co-morbidities: **1) & 2)** (n = 292) Hyper-coagulability - 16.4% Patient Details: Not stated Previous Treatment: Not stated

Authors/ Location	Intervention	Study Design	Study Population
Sakuda et al.[53] Second Department of Surgery, Faculty of Medicine, University of the Ryukyus, Okinawa, Japan	**1) SVS** Surgical Access: Not stated Anaesthesia: Not stated Surgical Technique: SVS consisted of interruption of the incompetent GSV, SSV, and perforators. The GSV was usually stripped from the knee to the thigh. When the maximum GSV diameter was less than 10 mm, it was ligated at both the saphenofemoral junction and below the knee. Incompetent perforators in the thigh and leg were interrupted with SEPS in legs with ulcerations, broad pigmentation or LDS; otherwise, a direct incision with multiple venotomies was performed. *SVS:* GSV stripping - 78.6%; GSV ligation - 21.4%; SSV stripping - 7.1%; SSV ligation - 92.9%; Perforator ligation - 92.9%; SEPS - 7.1%; Number of interrupted perforators - 2.6 (SD ± 0.9) Intra-operative Assessment of Venous/Valvular Competence: Not stated Vein Clamping: Not stated Anti-thrombotic Protocol: Not stated Adjunctive Surgery: No Post-operative Management: Not stated Operation Type: Not stated Preoperative Evaluation: Ascending and descending phlebography, duplex scanning Post-operative Evaluation: Air plethysmography, duplex scanning **2) SVS (as for group 1 above) plus external valvuloplasty** Surgical Access: Not stated Anaesthesia: Not stated	Prospective non-randomised concurrently controlled trial Level of Evidence: III-2 Intention-to-Treat Analysis: Not stated but intention-to-treat analysis conducted by default since there were no losses to follow-up. Participation Rate: Not stated Eligibility Rate for Study: Not stated Mean Follow-up: 25 months (range 12 to 37) Lost to Follow-up: 0% Study Period: 12/98 to 02/01 Operator Details: All post-operative air plethysmography measurements were done by the same physician. Inclusion Criteria: CVI caused by chronic valvular incompetence of the deep, saphenous and perforator veins. Exclusion Criteria: Post-thrombotic syndrome, clinical history of DVT, recurrent varicose veins/ulcers after stripping	Sample Size: (n = 25 patients) **1)** n = 14 limbs; **2)** n = 17 limbs No statistically significant difference between groups 1 and 2 in age, sex distribution, or venous filling index. However, the ratio of patients with CEAP classification C4 to C6 was significantly higher in group 2 than group 1 ($p < 0.01$). Patient Diagnosis: CVI caused by chronic valvular incompetence of the deep, saphenous and perforator veins. General Diagnostic Definitions: Deep venous incompetence was defined as the presence of moderate to severe reflux of grade 3 or 4 with the Herman and Kistner classifications on descending phlebography, performed according to the Thomas method. If reflux occurred ten or more seconds after the beginning of the injection the femoral venous valves were defined as competent. Valves with reflux time of more than 0.5 seconds on duplex scanning were considered incompetent. Preoperative Mean AVP: Not stated Preoperative Mean Refill Time: Not stated Preoperative Mean Maximum Venous Outflow: Not stated Type of Incompetence: **1) & 2)** Mixed superficial/perforator/deep Distribution of Incompetence: Not stated

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Authors/ Location	Intervention	Study Design	Study Population
	Surgical Technique: *SVS:* GSV stripping - 82.4%*; GSV ligation - 17.7%; SSV stripping - 0%; SSV ligation - 100%*; Perforator ligation - 23.5%; SEPS - 76.5%[§]; Number of interrupted perforators - 2.4 (SD ± 1.0)* *Valvuloplasty:* The femoral vein bifurcation or popliteal vein was dissected in the distal thigh. Once incompetence of the femoral vein valves was confirmed, an intra-operative angioscope was inserted into the femoral vein through a small oblique venotomy in the direction of venous flow, about 5 cm below the target valve. Several 7-0 polypropylene sutures were placed on both sides of the vein wall at the level of the commissure to shorten the valve cusps. The valvular sinus was then plicated to about 70% of its original outer diameter with a 7-0 polypropylene purse-string suture. The angioscope was then removed and the venotomy closed with 7-0 polypropylene interrupted sutures. Femoral vein valvuloplasty - 82.4%; Popliteal vein valvuloplasty - 17.7% Intra-operative Assessment of Venous/Valvular Competence: Not stated Vein Clamping: Not stated Anti-thrombotic Protocol: Systemic heparinisation Adjunctive Surgery: No Post-operative Management: Mild anti-coagulation therapy with warfarin was started the day after the procedure and continued for three months. Operation Type: Not stated Preoperative Evaluation: Ascending and descending phlebography, duplex scanning Post-operative Evaluation: Ascending and descending phlebography, air plethysmography, duplex scanning		Mean Age: **1)** 56.0 yrs (SD ± 13.0) (range 33 to 77) **2)** 56.0 yrs (SD ± 11.0) (range 39 to -80) Gender Mix: **1)** M/F = 8 (57.1%)/ 6 (42.9%) **2)** M/F = 8 (47.1%)/ 9 (52.9%) Clinical Grading: *CEAP Classification:* **1)** C2 - 42.9%; C3 - 21.4%; C4 - 28.6%; C5 - 0%; C6 - 7.1% **2)** C2 - 0%; C3 - 0%; C4 - 70.6%; C5 - 11.8%; C6 - 17.7% *Kistner Classification:* **1) & 2)** III or IV - 100% Patient Co-morbidities: Not stated Patient Details: Not stated Previous Treatment: Not stated

*No statistically significant difference between the two interventions at $p \geq 0.05$; [§]Statistically significant difference between the two intervention groups at $p \leq 0.001$

Authors/ Location	Intervention	Study Design	Study Population
AbuRahma et al. [54] Department of Surgery, West Virginia University Health Sciences Center, Charleston, West Virginia, USA Department of Clinical Research, Pfizer Central Research, Groton, Connecticut, USA	**1) Crossover femoral vein sapheno-femoral bypass (CFVB)** Surgical Access: Not stated Surgical Technique: The normal contra-lateral saphenous vein is dissected to the required length. Its tributaries are ligated and it is then tunnelled across the supra-pubic fat pad and anastomosed to the femoral vein, distal to the femoral obstruction, with a 6-0 continuous polypropylene suture. Intra-operative Assessment of Venous/Valvular Competence: Not stated Vein Clamping: Partial occluding clamp applied to the femoral vein. Adjunctive Surgery: Subfascial ligation of perforators (8.3% of patients); partial split skin graft performed 2 months post-operatively (4.2%). **2) Sapheno-popliteal vein bypass (SPVB)** Surgical Access: Incision in the upper leg just medial to the medial border of the tibia. Surgical Technique: The popliteal vein and its branches are exposed. The saphenous vein is then isolated and its branches ligated and divided. The saphenous vein is transected and an end-to-side sapheno-popliteal is accomplished with a 5-0 or 6-0 cardiovascular suture. Intra-operative Assessment of Venous/Valvular Competence: Not stated Vein Clamping: Partial occluding clamp applied to the popliteal vein. Adjunctive Surgery: Subfascial ligation of perforators with simultaneous split skin grafting (10.5%)	Retrospective non-randomised comparative study (unclear if controls were concurrent or historical) Level of Evidence: III-3 Intention-to-Treat Analysis: Not stated but intention-to-treat analysis conducted by default since there were no losses to follow-up. Participation Rate: Not applicable Eligibility Rate for Study: Not stated Mean Follow-up: **1)** 61.2 months; **2)** 66.2 months Lost to Follow-up: **1) & 2)** 0% Study Period: 01/07/78 to 30/06/88 Operator Details: Not stated	Sample Size: **1)** n = 24; **2)** n = 19 Statistical comparison of preoperative parameters for groups 1 and 2 was not reported. Patient Diagnosis: CVI caused by deep venous obstruction General Diagnostic Definitions: Normal maximum venous outflow is ≥ 20 mL/100 g of tissue/minute; normal venous refill time is ≥ 20 seconds; normal AVP was defined as a ≥ 50% fall in pressure during exercise with a recovery time of ≥ 20 seconds. Preoperative Mean AVP: Not stated Preoperative Mean Refill Time: **1)** 21.7 seconds; **2)** 20.3 seconds Preoperative Mean Maximum Venous Outflow: **1)** 16.2 mL; **2)** 17.1 mL Type of Incompetence: **1) & 2)** Deep - 100% Distribution of Incompetence: Not stated Mean Age: **1)** 47.1 yrs; **2)** 45.7 yrs Gender Mix: **1)** M/F = 9 (37.5%)/ 15 (62.5%) **2)** M/F = 6 (31.6%)/ 13 (68.4%) Clinical Grading*: **1)** Class II - 29.2%; Class III - 70.8% **2)** Class II - 26.3%; Class III - 73.7%

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Authors/ Location	Intervention	Study Design	Study Population
	1) & 2) Anaesthesia: Epidural or spinal anaesthesia Anti-thrombotic Protocol: Dextran 40 (100 mL bolus then 25 mL/hr intravenously up to 72 hours) was started at the beginning of surgery; 5,000 to 10,000 U of heparin was administered intravenously before venotomy. Sodium warfarin was started the night of surgery and continued for at least six months. Post-operative Management: An elastic compression stocking was used perioperatively. Post-operatively, patients used intermittent leg elevation during the day and elastic compression stockings with a compression of 30 to 50 mmHg at the ankle level. Sodium warfarin was continued for at least six months. Operation Type: Not stated Preoperative Evaluation: Strain gauge plethysmography, photoplethysmography, foot venous pressure measurement with calf exercise, venous valvular incompetency testing with a bi-directional ultrasound flow meter, ascending phlebography, duplex venous ultrasonography (last 3 years of the study) Post-operative Evaluation: Strain gauge plethysmography, photoplethysmography, bi-directional Doppler examination, ascending phlebography, duplex venous ultrasonography (last 3 years of the study)	Inclusion Criteria: CVI caused by deep venous obstruction Specific Surgical Inclusion Criteria: **CFVB**: 1) A patent, competent GSV on the run-off side with no varicosities 2) Inactive DVT for ≥ 6 months 3) Failure of conservative therapy continued for ≥ 12 months 4) Patent contra-lateral iliofemoral and caval run-off, and a patent deep femoral vein, preferably with an open or partially re-canalised SFV. **SPVB**: 1) A patent, competent GSV on the recipient side with no varicosities 2) Inactive DVT for ≥ 6 months 3) Failure of conservative therapy continued for ≥ 12 months 4) An isolated occlusion of the SFV and/or popliteal vein in the presence of patent tibial veins 5) Patent contra-lateral iliofemoral and caval run-off Exclusion Criteria: Not stated	Patient Co-morbidities: **1)** Compressed iliac vein - 20.8%; Claudication - 50.0% **2)** Compressed iliac vein - 0%; Claudication - 26.3% Patient Details: **1)** History of DVT - 66.7% **2)** History of DVT - 63.2% Previous Treatment: **1)** Pressure gradient stockings for ≥ 12 months - 29.2%; Compression therapy and local therapy for venous ulcerations - 70.8% **2)** Pressure gradient stockings for ≥ 12 months - 26.3%; Compression therapy and local therapy for venous ulcerations - 73.7%

*Class II (moderate CVI) included hyper-pigmentation of the skin in the gaiter area, moderate brawny edema, and sub-cutaneous fibrosis, which may be either limited in extent or involve the entire malleolar and pre-tibial area but without ulceration. Class III (severe CVI) was defined as chronic distal leg pain associated with ulcerative or pre-ulcerative skin changes, eczematoid changes, and/or severe edema.

Authors/ Location	Intervention	Study Design	Study Population
Cheatle & Perrin [55] Unite de Pathologie Vasculaire Jean Kunlin, Clinique du Grand-Large, Decines Charpieu, France	**1) SFV valvuloplasty** Surgical Access: Not stated Surgical Technique: The valve nearest the junction of the superficial and profunda femoral vein was repaired. The valve cusps were reefed with 7-0 Prolene, via a T-shaped venotomy, until competent. Intra-operative Assessment of Venous/Valvular Competence: Confirmed by the milking test conducted in the presence of raised intra-abdominal pressure Vein Clamping: Not stated Adjunctive Surgery: GSV and/or SSV stripping - 37.5%; GSV and/or SSV stripping plus perforator ligation - 62.5% (stripping was performed at least one week prior to valvuloplasty whereas ligation was performed at the same time as valvuloplasty) Operation Type: Unilateral **2) Transplantation** Surgical Access: Not stated Surgical Technique: (n = 27 limbs) Axillary vein interposed into the SFV - 55.6%; Contra-lateral GSV into the SFV - 18.5%; Axillary vein into the profunda femoris vein - 3.7%; Axillary vein into the popliteal vein - 11.1%; Contra-lateral SFV to the SFV - 11.1% Intra-operative Assessment of Venous/Valvular Competence: Not stated Vein Clamping: Not stated Adjunctive Surgery: (n = 27 limbs) GSV and/or SSV stripping - 18.5%; GSV and/or SSV stripping plus perforator ligation - 51.9%; Perforator ligation - 14.8% (stripping was performed at least one week prior to valvuloplasty whereas ligation was performed at the same time as transplantation) Operation Type: Bilateral - 3.8%	Non-randomised comparative study (unclear if prospective or retrospective and whether controls were concurrent or historical) Level of Evidence: III-3 Intention-to-Treat Analysis: No - three patients were lost to follow-up and their data were not included in the final analysis. Seven additional patients were not included in the final analysis because they had not completed a minimum of 6 months follow-up. Participation Rate: Not stated Eligibility Rate for Study: Not stated Median Follow-up: **1)** 21 months (range 10 to 37) **2)** 51 months (range 12 to 78) **3)** 46 months (range 12 to 100) **4)** 24 months (range 21 to 40) Lost to Follow-up: **1)** 0%; **2)** 3.9%; **3)** 20%; **4)** 0% One patient in group 3 died from unrelated causes but reasons for the other losses to follow-up were not stated. Study Period: Started 1981 but end date was not stated.	Sample Size: **1)** n = 8; **2)** n = 26 (27 limbs); **3)** n = 10; **4)** n = 9 Statistical comparison of preoperative parameters for the patient groups was not reported. Patient Diagnosis: Clinical and radiological evidence of post-thrombotic syndrome that was uncontrolled by conventional conservative treatment. General Diagnostic Definitions: Not stated Preoperative Mean AVP: Unable to derive raw data from graphical presentation Preoperative Mean Refill Time: Unable to derive raw data from graphical presentation Preoperative Mean Maximum Venous Outflow: Not stated Type of Incompetence: **1), 2), 3) & 4)** Secondary - 100% Distribution of Incompetence : Not stated Mean Age: **1)** 59 yrs (range 45 to 69); **2)** 51 yrs (range 24 to 73); **3)** 49 yrs (range 37 to 72); **4)** 53 yrs (range 40 to 63) Gender Mix: **1)** M/F = 2 (25.0%)/ 6 (75.0%) **2)** M/F = 9 (34.6%)/ 17 (65.4%) **3)** M/F = 5 (50.0%)/ 5 (50.0%) **4)** M/F = 5 (55.6%)/ 4 (44.4%)

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Authors/ Location	Intervention	Study Design	Study Population
	3) Transposition Surgical Access: Not stated Surgical Technique: In 70% of patients the SFV was divided close to its junction with the profunda femoris vein and anastomosed to the GSV below a competent saphenous valve. In 30% of patients the SFV was transposed to the competent profunda femoris vein. Intra-operative Assessment of Venous/Valvular Competence: Not stated Vein Clamping: Not stated Adjunctive Surgery: GSV and/or SSV stripping - 20.0%; GSV and/or SSV stripping plus perforator ligation - 40.0%; Perforator ligation - 20.0% (stripping was performed at least one week prior to valvuloplasty whereas ligation was performed at the same time as transposition) Operation Type: Unilateral **4) Psathakis sling procedure** Surgical Access: Not stated Surgical Technique: A Silastic sling was sutured to the gracilis tendon, passed between the popliteal vein and artery and fed medially for anchoring to the tendon of biceps femoris. The sling occludes the popliteal vein when the hamstring contracts, thus acting as an external valve and preventing retrograde flow. Intra-operative Assessment of Venous/Valvular Competence: Not stated Vein Clamping: Not stated Adjunctive Surgery: GSV and/or SSV stripping - 33.3%; Perforator ligation - 33.3% (stripping was performed at least one week prior to valvuloplasty whereas ligation was performed at the same time as the sling procedure) Operation Type: Unilateral	Operator Details: All operations were performed by a single surgeon. Inclusion Criteria: Not specifically stated Exclusion Criteria: Coagulopathy, rigid ankles	Clinical Grading (Kistner Classification): **1)** IV - 100%; **2)** (n = 27 limbs) III - 3.7%; IV - 96.3%; **3)** III - 10.0%; IV - 90.0%; **4)** IV - 100% Patient Co-morbidities: **1)** LDS, pain and swelling - 37.5%; **2)** (n = 27 limbs) LDS and pain - 18.5%; Pain and swelling - 7.4%; **3)** LDS - 10.0%; Pain and swelling - 20.0%; **4)** LDS - 11.1%; Pain and swelling - 11.1% Patient Details: **1)** History of recurrent ulceration - 62.5% **2)** (n = 27 limbs) History of recurrent ulceration - 74.1% **3)** History of recurrent ulceration - 70.0% **4)** History of recurrent ulceration - 77.8% Previous Treatment: **1)** Previous GSV and/or SSV stripping - 37.5% **2)** (n = 27 limbs) Previous GSV and/or SSV stripping - 55.6%; Previous GSV and/or SSV stripping plus perforator ligation - 11.1% **3)** Previous venous surgery - 0% **4)** Previous GSV and/or SSV stripping - 44.4%; Previous GSV and/or SSV stripping plus perforator ligation - 11.1%; Previous Palma procedure - 11.1%

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Authors/ Location	Intervention	Study Design	Study Population
	1), 2), 3) & 4) Anaesthesia: General Anti-thrombotic Protocol: Intra-operative systemic heparinisation Post-operative Management: Patients were anti-coagulated with intravenous heparin for 24 hours and then with oral vitamin K antagonists for 3 months. Intermittent pneumatic compression was used to prevent DVT until the patient was ambulant. Above-knee compression hosiery (grades II and III) is prescribed for 3 months, after which it is continued if clinically indicated. Preoperative Evaluation: Descending phlebography; and, since 1987, photoplethysmography, duplex scanning, and venous pressure measurements Post-operative Evaluation: Clinical assessment, ascending phlebography; photoplethysmography and duplex scanning (since 1987)		

Authors/ Location	Intervention	Study Design	Study Population
Danza et al. [56] Service of Vascular Surgery, Maciel Hospital, Montevideo, Uruguay	**1) Free femoro-femoral venous graft** Surgical Technique: The GSV of the donor leg is excised and re-anastomosed to the same vein and to the common femoral vein on the symptomatic side below the iliac obstruction. No further details were stated. **2) Saphenous vein transplant (Palma technique)** Surgical Technique: The GSV of the donor leg is freed long enough to reach the femoral vein of the recipient leg. The vein is then passed through a supra-pubic sub-cutaneous tunnel and anastomosed to the common femoral vein on the symptomatic side below the iliac obstruction. No further details were stated. **3) *In situ* sapheno-popliteal bypass** Surgical Technique: The GSV below the obstruction site is mobilised and anastomosed to the popliteal vein or to one of the tibial veins. The upper portion of the GSV and its arch are left *in situ*. A distal temporary arteriovenous fistula was employed in two patients (25.0%). No further details were stated. **4) Free femoro-femoral venous graft (as for group 1 above) plus *in situ* sapheno-popliteal bypass (as for group 3 above)** Surgical Technique: Temporary arteriovenous fistulas were employed at the level of the ankle for eight weeks. No further details were stated.	Non-randomised comparative study (unclear if prospective or retrospective and whether controls were concurrent or historical) Level of Evidence: III-3 Intention-to-Treat Analysis: Not stated but intention-to-treat analysis conducted by default since there were no losses to follow-up. Participation Rate: Not stated Eligibility Rate for Study: Not stated Follow-up: Not stated Lost to Follow-up: 0% Study Period: 1968 to 1987 Operator Details: Not stated Inclusion Criteria: Patients with chronic venous obstruction of the lower limbs in whom medical treatment had failed. Exclusion Criteria: Not stated	Sample Size: **1)** n = 19; **2)** n = 8; **3)** n = 8; **4)** n = 2; **5)** n = 3; **6)** n = 3 Statistical comparison of preoperative parameters for the patient groups was not reported. Patient Diagnosis: **1) & 2)** Iliac vein thrombosis; **3)** SFV thrombosis; **4)** Iliac vein thrombosis associated with SFV thrombosis; **5)** Obstruction of the common femoral vein due to iatrogenic ligature; **6)** Cavo-iliac thrombosis General Diagnostic Definitions: Not stated Preoperative Mean AVP: Not stated Preoperative Mean Refill Time: Not stated Preoperative Mean Maximum Venous Outflow: Not stated Type of Incompetence: Not stated Distribution of Incompetence : Not stated Mean Age: Not stated Gender Mix: Not stated Clinical Grading: Not stated Patient Co-morbidities: Not stated Patient Details: **1) to 6)** Progressive edema of the limbs in all cases - 100%; Incapacitating venous claudication - 70%; Trophic lesions - 35%.

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Authors/ Location	Intervention	Study Design	Study Population
	5) Femoro-iliac venous bypass Surgical Technique: Bypass from the superficial vein to the patent external iliac vein was performed using the contra-lateral GSV. No further details were stated. **6) Femoro-axillary bypass** Surgical Technique: Femoro-axillary venous bypass using the long GSV and an arm vein as the graft. A temporary groin arteriovenous fistula was also used. No further details were stated. **1) to 6)** Anti-thrombotic Protocol: Intra-operative heparin Adjunctive Surgery: No Post-operative Management: Dicoumarin was administered post-operatively for 4 to 6 months. Operation Type: Not stated Preoperative Evaluation: Ascending phlebography and, in recent years, Doppler ultrasound and strain-gauge plethysmography Post-operative Evaluation: Clinical assessment, ascending phlebography and, in recent years, Doppler ultrasound and strain-gauge plethysmography		Previous Treatment: All patients had unsuccessful treatment with exercise and application of elastic bandages for a minimum of 4 to 5 months.

Authors/ Location	Intervention	Study Design	Study Population
Iafrati et al. [57] Division of Vascular Surgery, New England Medical Center, Tufts University School of Medicine, Boston, Massachusetts, USA	**1) SEPS** Surgical Access: Two incisions were placed in the upper calf outside the limit of LDS. The first was placed 2 cm from the edge of the tibia and at least 10 cm distal to the tibial tuberosity. The second was placed 5 cm lateral and distal to the first incision. Surgical Technique: The lower leg was positioned so that it was elevated and parallel to the table. A dissecting balloon was passed, via the first incision, through the fascia and distended with 200 to 300 mL of saline. The balloon was then removed and the leg exsanguinated with an Esmarch bandage. A pneumatic tourniquet was placed on the thigh and inflated to 300 mmHg. A 10 mm port was then placed in the initial incision and the subfascial tunnel expanded and maintained with CO_2 inflation at 15 mmHg. A 5 mm port was then placed into the second incision. The perforating veins were visualised by blunt or sharp dissection and clipped with a 5 mm endo-clip applicator. After interruption of all perforating veins the tourniquet was released and the ports removed. Number of interrupted perforators - 5.9 (SD ± 3.0) Intra-operative Assessment of Venous/Valvular Competence: Not applicable Vein Clamping: Not stated Operation Type: Not reported for the mixed superficial/perforator/deep venous insufficiency subgroup.	Prospective non-randomised comparative study (unclear whether controls were concurrent or historical) Level of Evidence: III-3 Intention-to-Treat Analysis: Not stated but intention-to-treat analysis conducted by default since there were no losses to follow-up. Participation Rate: Not stated Eligibility Rate for Study: Not stated Mean Follow-up: 6.9 months (SD ± 4.56; range 1 to 18) Lost to Follow-up: 0% Study Period: 12/94 to 08/96 Operator Details: Not stated Inclusion Criteria: Not stated Exclusion Criteria: Not stated	Sample Size: **1)** n = 9 limbs; **2)** n = 4 limbs; **3)** n = 1 limb The study comprised a total of 15 patients (18 limbs) but only the data for those who had mixed superficial/perforator/deep or deep venous insufficiency have been tabulated. Some preoperative measurements were only available for the combined patient pool of n = 15 (n = 18 limbs). **Note:** This article was reported as a case series study and, therefore, comparisons between surgical techniques were not made in the original article. However, provision of outcome data for all 15 patients (18 limbs) in the article enabled a secondary analysis of the data for this review. Statistical comparison of preoperative parameters for the patient groups was not reported. Patient Diagnosis: Not stated General Diagnostic Definitions: Venous insufficiency was defined by a combination of descending phlebography, duplex valve closure time (> 1.0 second), and air plethysmography (venous filling index > 2 seconds). Preoperative Mean AVP: Not stated

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Authors/ Location	Intervention	Study Design	Study Population
	2) SEPS (as for group 1 above) plus SVS Surgical Access: The proximal and distal incisions for vein exposure were made before SEPS. Surgical Technique: Flush ligation and stripping of the GSV to below the knee was performed after SEPS. Number of interrupted perforators - 3.3 (SD ± 1.3) Intra-operative Assessment of Venous/Valvular Competence: Not applicable Vein Clamping: Not stated Operation Type: Not reported for the mixed superficial/perforator/deep venous insufficiency subgroup. **3) SEPS (as for group 1 above) plus valvuloplasty and vein transposition** Surgical Access: Not stated Surgical Technique: Angioscopic valvuloplasty and a venous segment transposition. Number of interrupted perforators - 0. Intra-operative Assessment of Venous/Valvular Competence: Not stated Vein Clamping: Not stated Operation Type: Unilateral		Preoperative Mean Refill Time: Not stated Preoperative Mean Maximum Venous Outflow: Not stated Type of Incompetence: **1)** Primary - 11.1%; Secondary - 88.9%; **2)** Secondary - 100%; **3)** Secondary - 100% **1)** Superficial, deep, and perforator - 55.6%; Deep and perforator - 44.4%; **2)** Superficial, deep, and perforator - 100%; **3)** Superficial and deep - 100%; Distribution of Incompetence: **1)** GSV - 11.1%; SSV - 22.2%; Deep femoral vein - 55.6%; SFV - 55.6%; Popliteal - 77.8%; Common femoral - 22.2%; Inferior vena cava - 22.2%; Common iliac - 11.1%; **2)** GSV - 100%; SSV - 50.0%; Deep femoral vein - 25.0%; SFV - 50.0%; Popliteal - 100%; Common femoral - 25.0%; **3)** SSV, deep femoral vein, SFV and popliteal - 100% Mean Age (n = 15): **1), 2) & 3)** 52 yrs (range 42 to 65)

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Authors/ Location	Intervention	Study Design	Study Population
	1), 2) & 3) Anaesthesia: General or spinal Anti-thrombotic Protocol: A single dose of heparin was administered before surgery. Adjunctive Surgery: No Post-operative Management: All patients were instructed to continue wearing compression stockings for 3 months or until the ulcer was healed. Lifetime use of compression stockings was advocated for patients who had significant uncorrected deep venous insufficiency. Preoperative Evaluation: Physical examination, plethysmography, duplex imaging, phlebography Post-operative Evaluation: Physical examination, duplex imaging		Gender Mix (n = 15): **1), 2) & 3)** M/F = 8 (53.3%)/ 7 (46.7%) Clinical Grading (n = 18 limbs): *Porter Classification:* **1), 2) & 3)** IV - 11.1%; V - 11.1%; VI - 77.8% *CEAP Classification:* **1)** C5 - 11.1%; C6 - 88.9%; **2)** C5 - 25.0%; C6 - 75.0%; **3)** C6 - 100% Patient Co-morbidities: Not stated Patient Details (n = 18 limbs): **1), 2) & 3)** Mean duration of CVI - 12 yrs (range 6 to 25); Active ulceration - 77.8% Previous Treatment (n = 18 limbs): **1), 2) & 3)** Previous ligation or stripping of the GSV - 50.0%; Previous perforator ligation - 27.8%

Authors/ Location	Intervention	Study Design	Study Population
Masuda & Kistner [58] Department of Vascular Surgery, Straub Clinic and Hospital, Honolulu, USA	**1) Femoral vein valvuloplasty** Surgical Technique: Veins were opened by longitudinal venotomy and, under loupe magnification, reefing sutures were placed through the floppy valves to the adjacent vein wall. Operation Type: Not stated No further details were stated. **2) Transposition** Surgical Technique: The SFV was joined either to a competent profunda femoris or GSV. Operation Type: Not stated No further details were stated. **3) Transplantation** Surgical Technique: A segment of proximal SFV was replaced with a segment of axillary or brachial vein containing a competent valve. Operation Type: Not stated No further details were stated. **4) Valvuloplasty plus transposition** Surgical Technique: As for groups 1 and 2 above. Operation Type: Not stated No further details were stated.	Prospective non-randomised comparative study (unclear whether controls were concurrent or historical) Level of Evidence: III-3 Intention-to-Treat Analysis: Yes Participation Rate: Not applicable Eligibility Rate for Study: 51 of 81 procedures (63.0%). Thirteen procedures could not be evaluated because patients had either died or moved away and their data were not included in the final analysis. Seventeen additional procedures were not included in the final analysis because they had not completed a minimum of four years follow-up. Mean Follow-up: 10.6 years (range 4 to 21 years) Lost to Follow-up: 0% Study Period: 1968 to 1990 Operator Details: Not stated	Sample Size: (n = 51 limbs) **1)** n = 32 limbs; **2)** n = 14 limbs; **3)** n = 2 limbs; **4)** n = 3 limbs Some preoperative measurements were only available for the combined patient pool of n = 48 (n = 51 limbs). Statistical comparison of preoperative parameters for the patient groups was not reported. Patient Diagnosis: Reflux disease in patients with CVI General Diagnostic Definitions: AVP was considered normal if the fall in pressure after exercise exceeded 50% of the pre-exercise pressure and the recovery time was > 20 seconds. A post-operative result was considered 'abnormal but improved' if either the percentage drop in post-exercise pressure of the recover time improved by at least 50% of the difference between the preoperative and the predicted normal values but did not fulfil the criteria of normal. All other results were classified as abnormal. Competence by duplex scanning was defined as duration of retrograde flow with Valsalva manoeuvre of ≤ 0.5 seconds; reflux was defined as retrograde flow lasting longer than 2.0 seconds. Retrograde flow between 0.5 and 2.0 seconds was considered mild reflux.

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Authors/ Location	Intervention	Study Design	Study Population
	1), 2), 3) & 4) Intra-operative Assessment of Venous/Valvular Competence: Assessed with the forceful strip test immediately after completion of the reconstruction. Adjunctive Surgery: Perforator interruption and saphenous vein ligation and stripping were performed selectively. All perforators greater than 3 to 4 mm were interrupted (35.3% of 51 limbs) and all incompetent saphenous veins were eliminated by ligation and stripping (47.1% of 51 limbs). However, no details of the number or distribution of patients that received adjunctive surgery were given. Post-operative Management: All patients were instructed to wear elastic support early in their post-operative course. Preoperative Evaluation: Clinical examination, hand-held Doppler scanner examination, photoplethysmography, ascending and descending phlebography. Post-operative Evaluation: Clinical examination, photoplethysmography (2 limbs), duplex scanning (31 limbs), descending phlebography (18 limbs), ascending phlebography	Inclusion Criteria: Not stated Exclusion Criteria: Not stated	Preoperative Mean AVP: Not stated Preoperative Mean Refill Time: **1)** (n = 7 limbs) 14.1 seconds (SD ± 6.3); **2)** (n = 11 limbs) 12.0 seconds (SD ± 6.0); **3)** (n = 2 limbs) 12.0 seconds (SD ± 2.8); **4)** (n = 2 limbs) 13.0 seconds (SD ± 4.2) Preoperative Mean Maximum Venous Outflow: Not stated Type of Incompetence: (n = 51 limbs) Primary deep venous insufficiency - 43.1%; Secondary deep venous insufficiency - 31.4%; Primary and secondary deep venous insufficiency - 25.5% (all patients in group 4 were in this category) Distribution of Incompetence: Not stated Mean Age: Not stated Gender Mix: Not stated Clinical Grading: **1), 2), 3) & 4)** (n = 51 limbs) Class 2* - 96.1%; Class 3* - 3.9% *Kistner Classification:* **1), 2), 3) & 4)** III or IV - 100%

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Authors/ Location	Intervention	Study Design	Study Population
			Patient Co-morbidities: Not stated Patient Details: **1), 2), 3) & 4)** (n = 51 limbs) Mean duration of symptoms - 8.3 yrs (± 6.0)†; All patients had either reflux from the common femoral vein to below the popliteal vein or from the common femoral vein to the distal tibial vein. Previous Treatment: **1), 2), 3) & 4)** (n = 51 limbs) Elastic support - 76.5%; Saphenous vein ligation and stripping - 29.4%; Perforator interruption - 5.9%

*Class 2 = presence of pre-ulcerative changes or moderate swelling, pain, or indurative symptoms; Class 3 = ulceration or severe, disabling swelling, pain or induration; †Paper did not define the variance measure used

Authors/ Location	Intervention	Study Design	Study Population
Owens et al.[59] Department of Surgery, Division of Vascular Surgery and Biostatistics, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, USA Department of Surgery, Fundacion Hospital de Alcorcon, Madrid, Spain	**1) SVS** Surgical Technique: Saphenous vein stripping with perforator ligation (53.3%) or without (46.7%). *Stripping:* Division and flush ligation of the GSV at the saphenofemoral junction or saphenopopliteal junction, followed by stripping from the groin with ligation of tributaries. Two patients also required SSV stripping. *Ligation:* Subfascial ligation of one to five perforating veins accomplished either by direct incision or SEPS. Operation Type: Not stated No further details were stated. **2) Transplantation** Surgical Access: Longitudinal incision in the groin Surgical Technique: A transverse venotomy was made in the recipient vein near the incompetent valve. Ten to twelve stay sutures of 5-0 Prolene were placed on the lower lip of the venotomy and weighted down by rubber-shod hemostats. An autogenous valve-bearing segment of axillary vein was transposed to the recipient vein and ensheathed in an 8 or 10 mm Dacron sleeve. Operation Type: Not stated No further details were stated. **1) & 2)** Preoperative Evaluation: Duplex ultrasound scan, air plethysmography Post-operative Evaluation: Air plethysmography	Non-randomised comparative study (unclear if prospective or retrospective and whether controls were concurrent or historical) Level of Evidence: III-3 Intention-to-Treat Analysis: No - results for 11 limbs were lost to follow-up and their data were not included in the final analysis. Participation Rate: Not stated Eligibility Rate for Study: Not stated Mean Follow-up: Not reported for the mixed superficial/perforator/deep venous insufficiency subgroup. Lost to Follow-up: 15.1%. No further details of were stated. Study Period: 12/91 to 09/99 Operator Details: Not stated Exclusion Criteria: Arterial insufficiency indicated by the presence of palpable pedal pulses or an ankle-brachial index > 0.8.	Sample Size: **1)** n = 15 limbs; **2)** n = 7 limbs The study comprised a total of 71 patients (73 limbs) but only the data for those who had mixed superficial/perforator/deep or deep venous insufficiency have been tabulated. Statistical comparison of preoperative parameters for the patient groups was not reported. Patient Diagnosis: CVI General Diagnostic Definitions: A cut-off valve closure time of 0.5 seconds was the criterion for significant reflux on duplex ultrasound scan. Preoperative Mean AVP: Not stated Preoperative Mean Refill Time: Not stated Preoperative Mean Maximum Venous Outflow: Not stated Type of Incompetence: **1)** Primary - 100%; **2)** Secondary - 100% **1)** Isolated deep venous insufficiency **2)** Deep and superficial or deep and superficial/perforator Distribution of Incompetence: Not stated Mean Age: Not stated Gender Mix: Not stated Clinical Grading (CEAP): **1) & 2)** C3 to C6 Patient Co-morbidities: Not stated Patient Details: Not stated Previous Treatment: Not stated

Authors/ Location	Intervention	Study Design	Study Population
Perrin [60]* Unite de Pathologie Vasculaire Jean Kunlin, Clinique du Grand-Large, Decines Charpieu, France	**1) SFV valvuloplasty** Surgical Technique: Internal valvuloplasty with phlebotomy at the end of the SFV was performed as a single procedure in 89.4% of limbs. In 3.5% of limbs internal valvuloplasty with phlebotomy at the end of the SFV was performed in combination with supplementary valvuloplasty with phlebotomy in the common femoral vein (1.2%) or the deep femoral vein (2.3%). In 7.1% of limbs internal valvuloplasty with phlebotomy at the end of the SFV was performed in combination with external supplementary valvuloplasty without phlebotomy in the popliteal vein. Adjunctive Surgery: SVS - 74.1%; Perforator ligation - 31.8%; Ligation of the end of the gastrocnemius veins - 20.0% (all procedures were performed a few days prior to deep venous surgery) Operation Type: Bilateral - 16.4% No further details were stated. **2) Transplantation** Surgical Technique: *Transplanted segment:* Axillary vein - 78.1%; Contra-lateral SFV - 9.4%; Contra-lateral GSV - 12.5% *Recipient site:* Ending of the SFV - 78.1%; Popliteal vein - 21.9% Adjunctive Surgery: SVS - 56.3%; Perforator ligation - 50.0%; Ligation of the end of the gastrocnemius veins - 6.3% (all procedures were performed a few days prior to deep venous surgery) Operation Type: Unilateral No further details were stated.	Retrospective non-randomised comparative study with mixed concurrent and historical controls Level of Evidence: III-3 Intention-to-Treat Analysis: No - patients were lost to follow-up and their data were not included in the final analysis. Participation Rate: Not stated Eligibility Rate for Study: Not stated Follow-up: **1)** 12 to 96 months **2)** 12 to 124 months **3)** 12 to 168 months **4)** Not clearly stated Lost to Follow-up: **1)** 4.7%; **2)** 6.3%; **3)** 11.1%; **4)** 33.3%‖ Reasons for the losses to follow-up were not stated. Study Period: 03/83 to 12/97 **1)** 1988 to 1997; **2)** 1984 to 1996; **3)** 1983 to 1997; **4)** 1988 to 1989 Operator Details: Not stated	Sample Size: (n = 133 patients) **1)** n = 85 limbs; **2)** n = 32 limbs; **3)** n = 18 limbs; **4)** n = 9 limbs Some preoperative measurements were only available for the combined patient pool of n = 133 (n = 144 limbs). There was a statistically significant difference between groups 1, 2 and 3 in clinical severity as defined by CEAP class (p = 0.01). Statistical comparison of other preoperative parameters for the patient groups was not reported. Patient Diagnosis: Deep venous reflux General Diagnostic Definitions: After release of distal compression of the calf a reflux of > 1.0 second on duplex scan was considered major, between 0.5 and 1.0 second as minor, and < 0.5 second as no reflux. Preoperative Mean AVP: Not stated Preoperative Mean Refill Time: Not stated Preoperative Mean Maximum Venous Outflow: Not stated Type of Incompetence: (n = 144 limbs) **1)** Primary - 76.5%; Primary and secondary - 22.4%; Klippel Trenaunay - 1.2%; **2)** Primary - 3.1%; Secondary - 96.9%; **3)** Primary - 11.1%; Secondary - 83.3%; Klippel Trenaunay - 5.6%; **4)** Secondary - 100.0%

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Authors/ Location	Intervention	Study Design	Study Population
	3) Transposition Surgical Technique: The ending of the SFV was transposed onto the GSV in 61.1% of limbs or onto the vertical branch of the deep femoral vein in 38.9%. When both the GSV and the deep femoral vein were competent the GSV was the vein of choice (22.2%). Adjunctive Surgery: SVS - 50.0%; Perforator ligation - 27.8% (all procedures were performed a few days prior to deep venous surgery) Operation Type: Unilateral No further details were stated. **4) Psathakis sling procedure** Surgical Technique: A Silastic sling was sutured to the gracilis tendon, passed between the popliteal vein and artery and fed medially for anchoring to the tendon of biceps femoris. The sling occludes the popliteal vein when the hamstring contracts, thus acting as an external valve and preventing retrograde flow. Adjunctive Surgery: SVS - 22.2%; Perforator ligation - 33.3% (all procedures were performed a few days prior to deep venous surgery) Operation Type: Unilateral No further details were stated.	Inclusion/Exclusion Criteria: Not specifically stated. However, contraindications for surgery were: severe, irreversible lesions affecting the muscular pumping system of the calf muscle; blockage of the tarsotibial joint after physical therapy or a neurological syndrome affecting the diseased limb; and the existence of a severe, permanent coagulation disorder.	Distribution of Incompetence : Not stated Mean Age: **1)** 50 yrs (range 27 to 77); **2)** 49 yrs (range 24 to 73); **3)** 46 yrs (range 27 to 72); **4)** 53 yrs (range 40 to 63) Gender Mix: **1)** (n = 73 patients) M/F = 43 (58.9%)/ 30 (41.1%) **2)** Data was not clearly presented **3)** M/F = 10 (55.6%)/ 8 (44.4%) **4)** M/F = 5 (55.6%)/ 4 (44.4%) Clinical Grading (CEAP Classification): (n = 144 limbs) **1)** Class 3 - 9.4%; Class 4 - 49.4%; Class 5,6 - 41.2%; **2)** Class 3 - 9.4%; Class 4 - 18.8%; Class 5,6 - 71.9%; **3)** Class 3 - 11.1%; Class 4 - 38.9%; Class 5,6 - 50.0%; **4)** Class 4 - 22.2%; Class 5,6 - 77.8% Patient Co-morbidities: Not stated Patient Details: Not stated Previous Treatment: All patients had previously undergone conservative management and/or venous surgery (saphenous vein stripping and/or perforator ligation).

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Authors/ Location	Intervention	Study Design	Study Population
	1), 2), 3) & 4) Post-operative Management: All patients underwent sequential compression therapy with monitoring (maximum pressure 30 mmHg) until they recovered from anaesthetic (4 to 6 hours). Intravenous heparin was administered (10 IU/kg every 24 hours) immediately in the post-operative period and then gradually increased until a complete anti-coagulant effect was achieved. Intravenous heparin was replaced with oral anti-coagulants on post-operative day five and continued for three months. Patients were forced to get out of bed the day after surgery and duration of ambulation was gradually increased with the use of elastic compression stockings. Preoperative Evaluation: Ascending and descending phlebography; combined continuous wave Doppler ultrasound until 1987, and subsequently pulsed wave Doppler ultrasonography; photoplethysmography since 1987 and air plethysmography since 1994 Post-operative Evaluation: Clinical assessment, ascending phlebography; Doppler ultrasonography; photoplethysmography since 1987 and air plethysmography since 1994		

*May include patients from Cheatle & Perrin [55] in its sample

‖The losses to follow-up for group 4 were poorly described and it was unclear whether this value was 33.3% or 55.6%

Authors/ Location	Intervention	Study Design	Study Population
Sottiurai [61] Department of Surgery, Section of Vascular Surgery, Louisiana State University Medical Center, New Orleans, Louisiana, USA	**1) SVS** Surgical Access: Vertical incision from the medial tibial condyle to the posterior medial malleolus. Anaesthesia: Not stated Surgical Technique: The crural fascia was reflected anteriorly to the anterior border of the tibia, and posteriorly beyond the SSV. Subfascial perforating veins were ligated with 3-0 silk prior to division. Both the GSV and the SSV were stripped when superficial valvular incompetence was present. Closure of the incision included re-approximation of the crural fascia with interrupted absorbable sutures, running subdermal continuous sutures, and subcuticular skin closure. Intra-operative Assessment of Venous/Valvular Competence: Not stated Vein Clamping: Not stated Anti-thrombotic Protocol: Not stated Adjunctive Surgery: No Operation Type: Not stated **2) SVS (as for group 1 above) plus valvuloplasty** Surgical Access: Vertical incision Anaesthesia: Not stated Surgical Technique: The distal SFV, popliteal vein or deep femoral vein was exposed. A transverse venotomy encompassing 60% of the circumference was made 2 to 3 mm above the valve commissures. A vertical venotomy from the mid-point of the transverse venotomy was extended into the valvular sinus. Vein flaps were retracted with 6-0 polypropylene or CV7 polytetrafluoroethylene sutures. The valve cusps were tacked to the wall at both of the commissures using 7-0 polypropylene or CV 8 polytetrafluoroethylene sutures. The vertical and transverse venotomies were closed with 6-0 polypropylene or CV7 polytetrafluoroethylene sutures.	Non-randomised comparative study (unclear if prospective or retrospective and whether controls were concurrent or historical) Level of Evidence: III-3 Intention-to-Treat Analysis: Not stated but intention-to-treat analysis conducted by default since there were no losses to follow-up. Participation Rate: Not stated Eligibility Rate for Study: Not stated Mean Follow-up: 37 months (range 10 to 73) Lost to Follow-up: 0% Study Period: 09/81 to 12/87 Operator Details: Not stated Inclusion Criteria: Recurrent leg ulcer refractory to non-surgical treatment, compliant to pre and post-operative treatment protocol, and incompetent perforator and deep venous valve demonstrated by phlebography Exclusion Criteria: Not stated	Sample Size: (n = 46 patients) **1)** n = 33 limbs; **2)** n = 21 limbs; **3)** n = 14 limbs; **4)** n = 8 limbs Some preoperative measurements were only available for the combined patient pool of n = 46 (n = 76 limbs). Statistical comparison of preoperative parameters for the patient groups was not reported. Patient Diagnosis: Superficial and deep venous valve incompetence with recurrent ulcer. General Diagnostic Definitions: An intra-operative venous pressure measurement via the dorsalis vein with and without Valsalva manoeuvre with the patient in a 45° reversed Trendelenburg position was performed. A venous pressure increment with Valsalva manoeuvre signified valvular incompetence. Preoperative Mean AVP: Unable to derive raw data from graphical presentation Preoperative Mean Refill Time: Not stated Preoperative Mean Maximum Venous Outflow: Not stated Type of Incompetence: **1), 2), 3) & 4)** Mixed superficial/perforator/deep Distribution of Incompetence: **1)** Deep venous incompetence limited to the above knee level - 100% **2), 3) & 4)** Deep venous incompetence extending below the knee - 100% Mean Age: Not stated

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Authors/ Location	Intervention	Study Design	Study Population
	Intra-operative Assessment of Venous/Valvular Competence: Tested by digital pressure as well as venous pressure measurement via the dorsalis vein with and without Valsalva manoeuvre with the patient a 45° reversed Trendelenburg position before and after valvuloplasty. Vein Clamping: Not stated Anti-thrombotic Protocol: Systemic heparinisation with 5,000 U of heparin Adjunctive Surgery: No Operation Type: Not stated **3) SVS (as for group 1 above) plus vein transposition** Surgical Access: Not stated Anaesthesia: Not stated Surgical Technique: This technique was used in patients whose valves were damaged beyond repair. Veins with incompetent superficial or deep femoral valves were transposed end-to-side to the vein (superficial or deep femoral) with a competent valve. In the presence of valvular incompetence in both the deep and the superficial femoral veins, a combined valvuloplasty and vein transposition was performed. Intra-operative Assessment of Venous/Valvular Competence: The valve of the recipient vein was tested prior to transposition. Venous pressure measurement was taken via the dorsalis vein with and without Valsalva manoeuvre with the patient in a 45° reversed Trendelenburg position before and after transposition. Vein Clamping: Not stated Anti-thrombotic Protocol: Fully heparinised during the operation. Adjunctive Surgery: No Operation Type: Not stated		Gender Mix: **1), 2), 3) & 4)** M/F = 18 (39.1%)/ 28 (60.9%) Clinical Grading: Not stated Patient Co-morbidities: (n = 46) **1), 2), 3) & 4)** Recurrent phlebitis - 73.9%; Thrombosis - 13.0%; Caval interruption - 13.1% Patient Details: **1), 2), 3) & 4)** Antithrombin III deficiency - 21.7%; Protein C deficiency - 6.5% Previous Treatment: **1), 2), 3) & 4)** Elastic stocking or ace wrap, cast, Unna boot, wet to dry dressing, intermittent compression pneumatic boot

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Authors/ Location	Intervention	Study Design	Study Population
	4) SVS (as for group 1 above) plus valve transplantation Surgical Access: Not stated Anaesthesia: Not stated Surgical Technique: This technique was used in patients whose valves were damaged beyond repair. A 5 cm long segment of vein with the valve in the mid-portion was excised from the proximal arm. End-to-end anastomosis was completed with spatulation and frequent interruptions at the suture line to avert stricture and purse-string sutures. Valvuloplasty of the arm vein was performed, when necessary, to restore competence in the incompetent transplanted valve. Intra-operative Assessment of Venous/Valvular Competence: The arm vein was tested for valve competence before harvesting and after transplantation. Tested by venous pressure measurement via the dorsalis vein with and without Valsalva manoeuvre with the patient in a 45° reversed Trendelenburg position before and after transplantation. Vein Clamping: Not stated Anti-thrombotic Protocol: Fully heparinised during the operation. Adjunctive Surgery: No Operation Type: Not stated **1), 2), 3) & 4)** Post-operative Management: Physical therapy to reduce hyperflexion of the foot was started on the second post-operative day. Intermittent compression with pneumatic boots for 4 to 6 hours per day was initiated on the second post-operative day and continued for a minimum of six months. Ambulation with medical grade elastic stockings was allowed after the SVS incision had healed. Patients in groups 2, 3, and 4 were maintained on low dose heparin for three days prior to discharge with a regimen of aspirin and dipyridamole. Patients with antithrombin III or protein C deficiency were placed on long-term Coumadin treatment. Preoperative Evaluation: Photoplethysmography, ascending and descending phlebography Post-operative Evaluation: Descending phlebography, photoplethysmography, clinical examination		

Authors/ Location	Intervention	Study Design	Study Population
Welch et al. 62 Division of Vascular Surgery, New England Medical Center Hospital, and Tufts University School of medicine, Boston, Massachusetts, USA	**1) Non-angioscopic valvuloplasty** Surgical Access: Longitudinal incision over the common and superficial femoral veins. Anaesthesia: Not stated Surgical Technique: The common and superficial femoral veins were dissected anteriorly and the valve leaflets identified. A transverse venotomy was then made just above the valve leaflets. The leaflets were reefed with interrupted 7-0 or 8-0 Prolene sutures. In two patients the repaired valves were wrapped with 6 mm thin walled polytetrafluoroethylene. Intra-operative Assessment of Venous/Valvular Competence: Strip test Vein Clamping: Occluding clamp Anti-thrombotic Protocol: Systemic heparinisation with a 5,000 U bolus of heparin Operation Type: Not stated **2) Angioscopic valvuloplasty** Surgical Access: Longitudinal incision over the common and superficial femoral veins. Anaesthesia: Not stated	Non-randomised comparative study (unclear if prospective or retrospective and whether controls were concurrent or historical) Level of Evidence: III-3 Intention-to-Treat Analysis: Not stated but intention-to-treat analysis conducted by default since there were no losses to follow-up. Participation Rate: Not stated Eligibility Rate for Study: Not stated Mean Follow-up: **1)** 32.5 months **2)** 10.6 months Lost to Follow-up: 0% Study Period: Not stated Operator Details: Not stated	Sample Size: (n = 6 patients) **1)** n = 4 limbs; **2)** n = 5 limbs Some preoperative measurements were only available for the combined patient pool of n = 6 (n = 9 limbs). Statistical comparison of preoperative parameters for the patient groups was not reported. Patient Diagnosis: CVI with venous ulcer. General Diagnostic Definitions: Not stated Preoperative Mean AVP: Not stated Preoperative Mean Refill Time: Not stated Preoperative Mean Maximum Venous Outflow: Not stated Type of Incompetence: Not stated Distribution of Incompetence: **1) & 2)** Deep femoral vein incompetence - 0%; further details not stated Mean Age: (n = 6) **1) & 2)** 49 yrs (range 32 to 62) Gender Mix: (n = 6) **1) & 2)** M/F = 4 (66.7%)/ 2 (33.3%)

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Authors/ Location	Intervention	Study Design	Study Population
	Surgical Technique: The common and superficial femoral veins were dissected anteriorly and the valve leaflets identified. The angioscope was inserted through a large tributary of the proximal GSV or femoral vein down into the SFV. After valve incompetence was confirmed, a transverse venotomy was made just above the valve leaflets. The leaflets were then reefed with interrupted 7-0 or 8-0 Prolene sutures. The venotomy was then closed and the angioscope re-inserted to observe valve competence. If needed, an additional suture was added to render the valve competent. In two patients, valvuloplasty was performed without venotomy by placing the angioscope within the vein lumen to visualise and guide suture placement across the valve commissures. Intra-operative Assessment of Venous/Valvular Competence: Angioscopic visualisation Vein Clamping: Not stated Anti-thrombotic Protocol: Not stated Operation Type: Not stated **1) & 2)** Adjunctive Surgery: (n = 9 limbs) Subfascial ligation of incompetent perforating veins - 55.6%; Ligation and stripping of superficial varicosities - 33.3%; External banding of the valvuloplasty with a polytetrafluoroethylene sheath - 22.2% Post-operative Management: All but the initial two patients were treated with heparin and pneumatic compression boots in the immediate post-operative period, with subsequent conversion to warfarin therapy for six months. Elastic compression stockings were worn for at least six months after surgery. Preoperative Evaluation: Ascending and descending phlebography, light reflection rheography, air plethysmography, duplex scanning Post-operative Evaluation: Ascending and descending phlebography, light reflection rheography, air plethysmography, duplex scanning	Inclusion Criteria: Not stated Exclusion Criteria: Not stated	Clinical Grading: *Society for Vascular Surgery/International Society for Cardiovascular Surgery:* (n = 9 limbs) **1) & 2)** Stage III - 100% *Kistner Classification:* (n = 9 limbs) **1) & 2)** II - 22.2%; III-11.1%; IV -66.7% Patient Co-morbidities: Not stated Patient Details: **1) & 2)** Duration of venous ulcers - range 2 to 10 years Previous Treatment: **1) & 2)** Compression stockings or Unna boots - 100%; Previous ligation and stripping of superficial varicose veins - 55.6%

Efficacy Outcomes - RCTs

	Belcaro et al. [51] (Level II)		Makarova et al. [50] (Level II)	
Perioperative Outcomes	**SVS n = 18**	**SVS plus LAP n = 17**	**SVS n = 62**	**SVS plus valvuloplasty n = 63**
Mean time to ambulation (hours)		< 7 (n = 22)		
Mean hospital stay (hours)		8 ⌈4⌋ (n = 22)		
Intra-operative venous competence		100%		
Post-operative Outcomes	**FU = 10 years**		**FU range = 7 to 8 years**	
Increase in clinical class			24.2%	9.5%
No change in clinical class			64.5%	85.7%
Recurrent varicosities			11.3%	4.8%††
Persistence of reflux			46.8%	
Increase in reflux			53.2%	15.9%
Decrease in reflux			0%	71.4%
Reflux recurrence				19.1%
Recurrence plus increase of reflux				12.7%
Competent SFV vein	0%	100%		71.4%
Change in mean QOL score	↓25.0%‖	↓77.6%‖†#‡‡		

†Statistically significant difference between the two surgical techniques at $p \leq 0.05$
‖Statistically significant difference compared to baseline at $p \leq 0.05$
††The overall difference between the two groups in terms of recurrence rate and change in clinical class was significant at $p < 0.05$
⌈⌋ = Paper did not define the variance measure used
‡‡Measured on a visual analog scale; for each item the score ranged from 0 (no problem) to 10 (most severe)

Post-operative Venous Function - RCTs

	Belcaro et al. [51] (Level II)	
Venous Function Measures	**SVS n = 18**	**SVS plus LAP n = 17**
End Of Study Outcome Relative To Baseline	**FU = 10 years**	
Change in mean AVP (without ankle tourniquet)	↓4.6%	↓32.3%†
Change in mean refill time (without ankle tourniquet)	↑20.0%	↑77.8%†
Change in mean AVP (with ankle tourniquet)	↓16.1%	↓26.2%†
Change in mean refill time (with ankle tourniquet)	↑18.2%	↑54.6%†
Change in mean femoral vein diameter	↑8.3%	↓26.8%‖

†Statistically significant difference between the two surgical techniques at $p \leq 0.05$
‖Statistically significant difference compared to baseline at $p \leq 0.05$

Safety Outcomes - RCTs

	Belcaro et al. [51] (Level II)	
Post-operative Outcomes	**SVS n = 18**	**SVS plus LAP n = 17**
	FU = 10 years	
Complications	0%	0%
Superficial vein thrombosis	0%	0%
DVT	0%	0%

Efficacy Outcomes - Non-randomised comparative studies

	Jamieson & Chinnick [29] (Level III-2)		Raju et al. [52] (Level III-2)		Sakuda et al. [53] (Level III-2)		AbuRahma et al. [54] (Level III-3)	
Perioperative Outcomes	**Valvulo-plasty n = 12 limbs**	**Trans-plantation n = 4 limbs**	**Stenting n = 243 limbs**	**Stenting plus SVS n = 61 limbs**	**SVS n = 14 limbs**	**SVS plus valvuloplasty n = 17 limbs**	**CFVB n = 24**	**SPVB n = 19**
Mean hospital stay (days)	Combined groups = 5 to 7		Combined groups < 1					
Post-operative Outcomes	**FU = ≥ 2 years**		**Mean FU = 9 mths**		**Mean FU = 25 mths**		**FU = 61.2 mths**	**FU = 66.2 mths**
Improvement in clinical class/status						94.1% (at discharge)	62.5%	57.9%
Deterioration in clinical class/status							4.2%	5.3%
No change in clinical class/status						5.9% (at discharge)	33.3%	36.8%
Asymptomatic	8.3%							
Improvement in symptoms	83.3%	75.0%						
Deterioration in symptoms								
No change in symptoms	8.3%	25.0%						
Severe reflux								
Major reflux		100% (n = 1)						
Minor reflux								
Competence or mild reflux								
No reflux	100% (n = 3)							
Reflux recurrence								
Vein/valve obstructed								
Vein/valve re-canalised								

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	Jamieson & Chinnick [29] (Level III-2)		Raju et al. [52] (Level III-2)		Sakuda et al. [53] (Level III-2)		AbuRahma et al. [54] (Level III-3)	
Post-operative Outcomes	**Valvulo-plasty n = 12 limbs**	**Trans-plantation n = 4 limbs**	**Stenting n = 243 limbs**	**Stenting plus SVS n = 61 limbs**	**SVS n = 14 limbs**	**SVS plus valvuloplasty n = 17 limbs**	**CFVB n = 24**	**SPVB n = 19**
Valve competence								
Vein/valve patency					28.6%	94.1%‡	75.0%	57.9%
Cumulative patency rate							75.0% (84 mths)	56.0% (93 mths)
Ten-year cumulative success rate								
Abnormal photoplethysmography							12.5% (FU ≥ 1 yr)	21.1% (FU ≥ 1 yr)
Abnormal strain gauge plethysmography							12.5% (FU ≥ 1 yr)	10.5% (FU ≥ 1 yr)
Abnormal maximum venous outflow							4.0%‖ (FU ≥ 1 yr)	11.0%‖ (FU ≥ 1 yr)
New ulcer occurrence					0%	0%		
Ulcer present prior to surgery			n = 37	n = 12				
Healed			59.5%	50%*				
Recurrent								
Worsening of varicose pigmentation					7.1%			
Continued need of external support					64.3%	23.5%†		
Change in mean venous clinical severity score					↓61.8%#	↓83.5%†#		
Change in mean venous disability score					↓33.3%#	↓63.6%†#		

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	Jamieson & Chinnick [29] (Level III-2)		Raju et al. [52] (Level III-2)		Sakuda et al. [53] (Level III-2)		AbuRahma et al. [54] (Level III-3)	
Post-operative Outcomes	**Valvulo-plasty n = 12 limbs**	**Trans-plantation n = 4 limbs**	**Stenting n = 243 limbs**	**Stenting plus SVS n = 61 limbs**	**SVS n = 14 limbs**	**SVS plus valvuloplasty n = 17 limbs**	**CFVB n = 24**	**SPVB n = 19**
Re-intervention rate								
Surgery to remove venous sling								
Crossover operation							4.2%	
Palma procedure								
Re-intervention required but refused							8.3%	15.8%

*No statistically significant difference between the interventions at $p \geq 0.05$
†Statistically significant difference between the interventions at $p \leq 0.05$; ‡$p \leq 0.01$
‖Statistically significant difference compared to baseline at $p \leq 0.05$; #$p \leq 0.001$

	Cheatle & Perrin [55] (Level III-3)				Danza et al. [56] (Level III-3)					
Perioperative Outcomes	**Valvulo-plasty n = 6**	**Trans-plantation n = 21**	**Trans-position n = 8**	**Sling procedure n = 9**	**Femoro-femoral graft n = 19**	**Trans-plantation n = 8**	**Sapheno-popliteal bypass n = 8**	**Femoro-femoral graft plus sapheno-popliteal bypass n = 2**	**Femoro-iliac bypass n = 3**	**Femoro-axillary bypass n = 3**
Mean hospital stay (days)										
Post-operative Outcomes	**Median FU = 21 mths**	**Median FU = 51 mths**	**Median FU = 46 mths**	**Median FU = 24 mths**	**FU = Not stated**					
Improvement in clinical class/status										
Deterioration in clinical class/status										
No change in clinical class/status										
Asymptomatic					63.2%	37.5%	37.5%		100.0%	
Improvement in symptoms	66.7%	47.6%	62.5%	77.8%	15.8%	37.5%	37.5%	100.0%		100.0%
Deterioration in symptoms										
No change in symptoms		52.4%	37.5%			21.1%	25.0%	25.0%		
Severe reflux										
Major reflux										
Minor reflux										
Competence or mild reflux										
No reflux										
Reflux recurrence		57.1%[††]	12.5%	66.7%						
Vein/valve obstructed	33.3%	28.6%	25.0%	22.2%						
Vein/valve re-canalised		23.8%								

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	Cheatle & Perrin [55] (Level III-3)				Danza et al. [56] (Level III-3)					
Post-operative Outcomes	**Valvulo-plasty n = 6**	**Trans-plantation n = 21**	**Trans-position n = 8**	**Sling procedure n = 9**	**Femoro-femoral graft n = 19**	**Trans-plantation n = 8**	**Saphena-popliteal bypass n = 8**	**Femoro-femoral graft plus saphena-popliteal bypass n = 2**	**Femoro-iliac bypass n = 3**	**Femoro-axillary bypass n = 3**
Valve competence	66.7%	9.5%	62.5%	11.1%						
Vein/valve patency	66.7%	57.1%	75.0%	11.1%						
Cumulative patency rate										
Ten-year cumulative success rate										
Abnormal photoplethysmography										
Abnormal strain gauge plethysmography										
Abnormal maximum venous outflow										
New ulcer occurrence										
Ulcer present prior to surgery	n = 3	n = 16	n = 6	n = 7						
Healed										
Recurrent	33% Median FU = 24 mths	31.3% Median FU = 48 mths	33.3% Median FU = 40 mths	28.6% Median FU = 24 mths						
Worsening of varicose pigmentation										
Continued need of external support										

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	Cheatle & Perrin [55] (Level III-3)				Danza et al. [56] (Level III-3)					
Post-operative Outcomes	**Valvulo-plasty n = 6**	**Trans-plantation n = 21**	**Trans-position n = 8**	**Sling procedure n = 9**	**Femoro-femoral graft n = 19**	**Trans-plantation n = 8**	**Sapheno-popliteal bypass n = 8**	**Femoro-femoral graft plus sapheno-popliteal bypass n = 2**	**Femoro-iliac bypass n = 3**	**Femoro-axillary bypass n = 3**
Change in mean venous clinical severity score										
Change in mean venous disability score										
Re-intervention rate										
Surgery to remove venous sling				11.1%**						
Crossover operation										
Palma procedure			12.5%							
Re-intervention required but refused										

**Due to chronic inflammation in the popliteal fossa; ††Four patients grafts that re-canalised after thrombosis

	Iafrati et al. [57††] (Level III-3)			Masuda & Kistner [58] (Level III-3)				Perrin [60] (Level III-3)			
Perioperative Outcomes	**SEPS n = 9 limbs**	**SEPS plus SVS n = 4 limbs**	**SEPS plus deep vein reconstruction n = 1 limb**	**Valvuloplasty n = 32 limbs**	**Transposition n = 14 limbs**	**Transplantation n = 2 limbs**	**Valvuloplasty plus transposition n = 3 limbs**	**Valvuloplasty n = 85 limbs**	**Transplantation n = 32 limbs**	**Transposition n = 18 limbs**	**Sling procedure n = 9 limbs**
Mean hospital stay (days)								Combined groups = 8.5 (range 6 to 15)			
Post-operative Outcomes	**Mean FU = 6.9 months**			**Mean FU = 10.6 years**				**FU = 12 to 96 mths**	**FU = 12 to 124 mths**	**FU = 12 to 168 mths**	**FU = Not stated**
Improvement in clinical class/status				71.9%	50.0%	0%	33.3%				
Deterioration in clinical class/status											
No change in clinical class/status					50.0%	100%	66.7%				
Asymptomatic	22.2%	25.0%		43.8%	21.4%	0%	0%				
Improvement in symptoms	66.7%	50.0%	100%								
Deterioration in symptoms	0%	0%	0%								
No change in symptoms	11.1%	25.0%									
Severe reflux				22.6%† (n = 31)	23.1%† (n = 13)	0%	100%†				
Major reflux								21.0% (n = 81)	53.3% (n = 30)	33.3% (n = 15)	
Minor reflux								16.0% (n = 81)	25.0% (n = 30)	6.7% (n = 15)	

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	Iafrati et al. [57††] (Level III-3)			Masuda & Kistner [58] (Level III-3)				Perrin [60] (Level III-3)			
Post-operative Outcomes	**SEPS n = 9 limbs**	**SEPS plus SVS n = 4 limbs**	**SEPS plus deep vein recon-struction n = 1 limb**	**Valvulo-plasty n = 32 limbs**	**Trans-position n = 14 limbs**	**Trans-plantation n = 2 limbs**	**Valvulo-plasty plus trans-position n = 3 limbs**	**Valvulo-plasty n = 85 limbs**	**Trans-plantation n = 32 limbs**	**Trans-position n = 18 limbs**	**Sling procedure n = 9 limbs**
Competence or mild reflux				77.4%† (n = 31)	76.9%† (n = 13)	100%†	0%				
No reflux								63.0% (n = 81)	26.7% (n = 30)	60% (n = 15)	
Reflux recurrence											
Vein/valve obstructed				3.1%**							
Vein/valve re-canalised											
Valve competence											
Vein/valve patency											
Cumulative patency rate											
Ten-year cumulative success rate				72.0%	Combined groups = 40.0%†						
Abnormal photoplethysmography											
Abnormal strain gauge plethysmography											
Abnormal maximum venous outflow											

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	Iafrati et al. [57††] (Level III-3)			Masuda & Kistner [58] (Level III-3)				Perrin [60] (Level III-3)			
Post-operative Outcomes	**SEPS n = 9 limbs**	**SEPS plus SVS n = 4 limbs**	**SEPS plus deep vein reconstruction n = 1 limb**	**Valvuloplasty n = 32 limbs**	**Transposition n = 14 limbs**	**Transplantation n = 2 limbs**	**Valvuloplasty plus transposition n = 3 limbs**	**Valvuloplasty n = 85 limbs**	**Transplantation n = 32 limbs**	**Transposition n = 18 limbs**	**Sling procedure n = 9 limbs**
New ulcer occurrence	0%	0%	0%								
Ulcer present prior to surgery	Not stated	Not stated	Not stated					n = 35	n = 23	n = 9	Not stated
Healed											
Recurrent	0%	0%	0%					22.9%[‡‡]	39.1%[‡‡]	22.2%[‡‡]	n = 4
Worsening of varicose pigmentation											
Continued need of external support											
Change in mean venous clinical severity score											
Change in mean venous disability score											
Re-intervention rate											
Surgery to remove venous sling											
Crossover operation											
Palma procedure											
Re-intervention required but refused											

[†]Statistically significant difference between the interventions at $p \leq 0.05$
**Identified 17 years after surgery; patient remained asymptomatic; [††]This article was reported as a case series study and, therefore, comparisons between surgical techniques were not made in the original article. However, provision of outcome data for all 15 patients (18 limbs) in the article enabled a secondary analysis of the data for this review.
[‡‡]Derived from life table curve of ulcer recurrence free survival

	Sottiurai [61] (Level III-3)				Welch et al. [62] (Level III-3)	
Perioperative Outcomes	**SVS n = 33 limbs**	**SVS plus valvuloplasty n = 21 limbs**	**SVS plus transposition n = 14 limbs**	**SVS plus trans-plantation n = 8 limbs**	**Valvuloplasty n = 4 limbs**	**Angioscopic valvuloplasty n = 5 limbs**
Mean hospital stay (days)						
Post-operative Outcomes	**Mean FU = 37 mths**				**Mean FU = 32.5 mths**	**Mean FU = 10.6 mths**
Improvement in clinical class/status						
Deterioration in clinical class/status						
No change in clinical class/status						
Asymptomatic						
Improvement in symptoms						
Deterioration in symptoms						
No change in symptoms						
Severe reflux						
Major reflux						
Minor reflux						
Competence or mild reflux						
No reflux						
Reflux recurrence						
Vein/valve obstructed						
Vein/valve re-canalised						
Valve competence		100% (FU = 3 mths)	85.7% (FU = 3 mths)	87.5% (FU = 3 mths)		
Vein/valve patency					100% (n = 3)	100%
Cumulative patency rate						

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	Sottiurai [61] (Level III-3)				Welch et al. [62] (Level III-3)	
Post-operative Outcomes	**SVS n = 33 limbs**	**SVS plus valvuloplasty n = 21 limbs**	**SVS plus transposition n = 14 limbs**	**SVS plus trans-plantation n = 8 limbs**	**Valvuloplasty n = 4 limbs**	**Angioscopic valvuloplasty n = 5 limbs**
Ten-year cumulative success rate						
Abnormal photoplethysmography						
Abnormal strain gauge plethysmography						
Abnormal maximum venous outflow						
New ulcer occurrence						
Ulcer present prior to surgery	n = 33	n = 21	n = 14	n = 8	n = 4	n = 5
Healed	42.4%	80.9%	78.6%	75.0%	100%	100%
Recurrent	57.6%	19.1%	21.4%	25.0%*	0%	0%
Worsening of varicose pigmentation						
Continued need of external support	81.8%	19.1%	21.4%	25.0%		
Change in mean venous clinical severity score						
Change in mean venous disability score						
Re-intervention rate						
Surgery to remove venous sling						
Crossover operation						
Palma procedure						
Re-intervention required but refused						

*No statistically significant difference between the intervention groups at $p \geq 0.05$

Post-operative venous function - Non-randomised comparative studies

	Sakuda et al. [53] (Level III-2)	
Venous Function Measures	**SVS n = 14 limbs**	**SVS plus valvuloplasty n = 17 limbs**
End Of Study Outcome Relative To Baseline	**Mean FU = 25 months**	
Change in mean refill time(without ankle tourniquet)		
Change in mean refill time(with ankle tourniquet)		
Change in mean maximum venous outflow		
Change in mean venous volume	↓15.5% (FU = 1 mth)	↓24.1%‡ (FU = 1 mth)
Change in mean venous filling index	↓25.5%¶ (FU = 1 mth)	↓68.2%¶‡‖ (FU = 1 mth)
Change in mean ejection fraction	↑37.0%** (FU = 1 mth)	↑18.3%** (FU = 1 mth)
Change in mean residual volume fraction	↓11.4%** (FU = 1 mth)	↓11.5%** (FU = 1 mth)

‡Statistically significant difference between the two intervention groups at $p \leq 0.01$
**No statistically significant difference compared to baseline at $p \geq 0.05$
¶Statistically significant difference compared to baseline at $p \leq 0.01$
‖This difference continued for more than two years after surgery ($p < 0.05$)

	AbuRahma et al. [54] (Level III-3)		Masuda & Kistner [58] (Level III-3)				Owens et al. [59] (Level III-3)	
Venous Function Measures	**CFVB n = 24**	**SPVB n = 19**	**Valvulo-plasty n = 7 limbs**	**Trans-position n = 11 limbs**	**Trans-plantation n = 2 limbs**	**Valvulo-plasty plus trans-position n = 2 limbs**	**SVS n = 15 limbs**	**Trans-plantation n = 7 limbs**
End Of Study Outcome Relative To Baseline	**FU ≥ 1 year**		**Mean FU = 10.6 years**				**Mean FU = Not stated**	
Change in mean refill time(without ankle tourniquet)			↑55.6%¶	↑73.4%¶	↓26.9%**	↑54.2%**		
Change in mean refill time(with ankle tourniquet)	↑8.3%	↑4.9%						
Change in mean maximum venous outflow	↑120.4%	↑156.1%						
Change in mean venous volume								
Change in mean venous filling index							↓50.5%	↓36.6%
Change in mean ejection fraction								
Change in mean residual volume fraction								

**No statistically significant difference compared to baseline $p \geq 0.05$
¶Statistically significant difference compared to baseline $p \leq 0.01$

Safety Outcomes - Non-randomised comparative studies

	Jamieson & Chinnick [29] (Level III-2)		Raju et al. [52] (Level III-2)		Sakuda et al. [53] (Level III-2)	
Post-operative Outcomes	**Valvuloplasty n = 12 limbs**	**Transplantation n = 4 limbs**	**Stenting n = 243 limbs**	**Stenting plus SVS n = 61 limbs**	**SVS n = 14 limbs**	**SVS plus valvuloplasty n = 17 limbs**
	FU ≥ 2 years		**Mean FU = 9 months**		**Mean FU = 25 months**	
Mortality (< 30 days)						
Mortality	0%	0%	0% FU = 6 wks	0% FU = 6 wks		
Major complications	0%	0%				
Complications			0%	0%	0%	0%
DVT	0%	0%			0%	0%
Pulmonary embolism						
Hemorrhage	0%	0%				
Wound infection					0%	5.9%*

*No statistically significant difference between the two interventions at p ≥ 0.05

	AbuRahma et al. [54] (Level III-3)		Cheatle & Perrin [55] (Level III-3)				Iafrati et al. [57] (Level III-3)		
Post-operative Outcomes	**CFVB n = 24**	**SPVB n = 19**	**Valvulo-plasty n = 6**	**Trans-plantation n = 21**	**Trans-position n = 8**	**Sling procedure n = 9**	**SEPS n = 9 limbs**	**SEPS plus SVS n = 4 limbs**	**SEPS plus deep venous reconstruction n = 1 limb**
	FU = 30 days		**Median FU = 21 mths**	**Median FU = 51 mths**	**Median FU = 46 mths**	**Median FU = 24 mths**	**Mean FU = 6.9 months**		
Mortality (< 30 days)	0%	0%							
Mortality									
Major complications									
Complications									
DVT	4.2%	5.3%	33.3%	28.6%	25.0%	22.2%			
Pulmonary embolism									
Hemorrhage									
Wound infection		5.3%						25.0%	

	Perrin [60] (Level III-3)				Welch et al. [62] (Level III-3)	
Post-operative Outcomes	**Valvuloplasty n = 85 limbs**	**Transplantation n = 32 limbs**	**Transposition n = 18 limbs**	**Sling procedure n = 9 limbs**	**Valvuloplasty n = 4 limbs**	**Angioscopic valvuloplasty n = 5 limbs**
	FU = 12 to 96 mths	**FU = 12 to 124 mths**	**FU = 12 to 168 mths**	**FU = Not stated**	**Mean FU = 32.5 mths**	**Mean FU = 10.6 mths**
Mortality (< 30 days)						
Mortality						
Major complications						
Complications						
DVT	12.9%	37.5%	27.8%	11.1%	50.0%‖	
Pulmonary embolism	0%	0%	0%	0%		
Hemorrhage						
Wound infection						

‖Both patients underwent external banded valvuloplasty and were not receiving anti-coagulants at the time of thrombosis.

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